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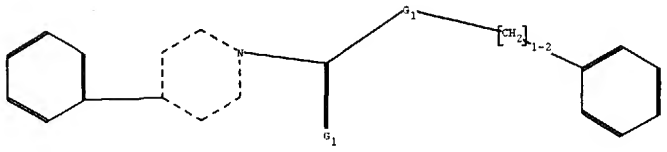

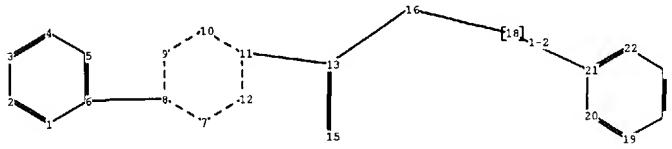

chain nodes :
13 15 16 18
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 19 20 21 22 23 24
chain bonds :
6-8 11-13 13-15 13-16 16-18 18-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 19-20 19-24 20-21
21-22 22-23 23-24
exact/norm bonds :
7-8 7-12 8-9 9-10 10-11 11-12 11-13 13-15 13-16 16-18
exact bonds :
6-8 18-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24
isolated ring systems :
containing 1 : 7 : 19 :

G1:O,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 15:CLASS 16:CLASS 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom
23:Atom 24:Atom

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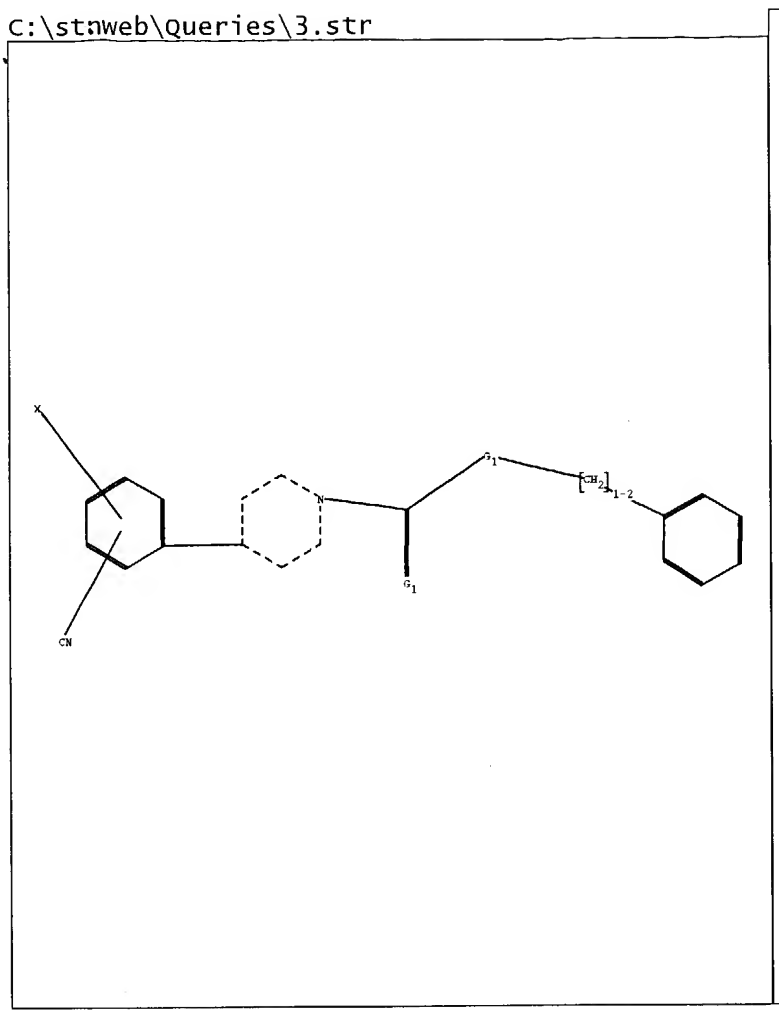

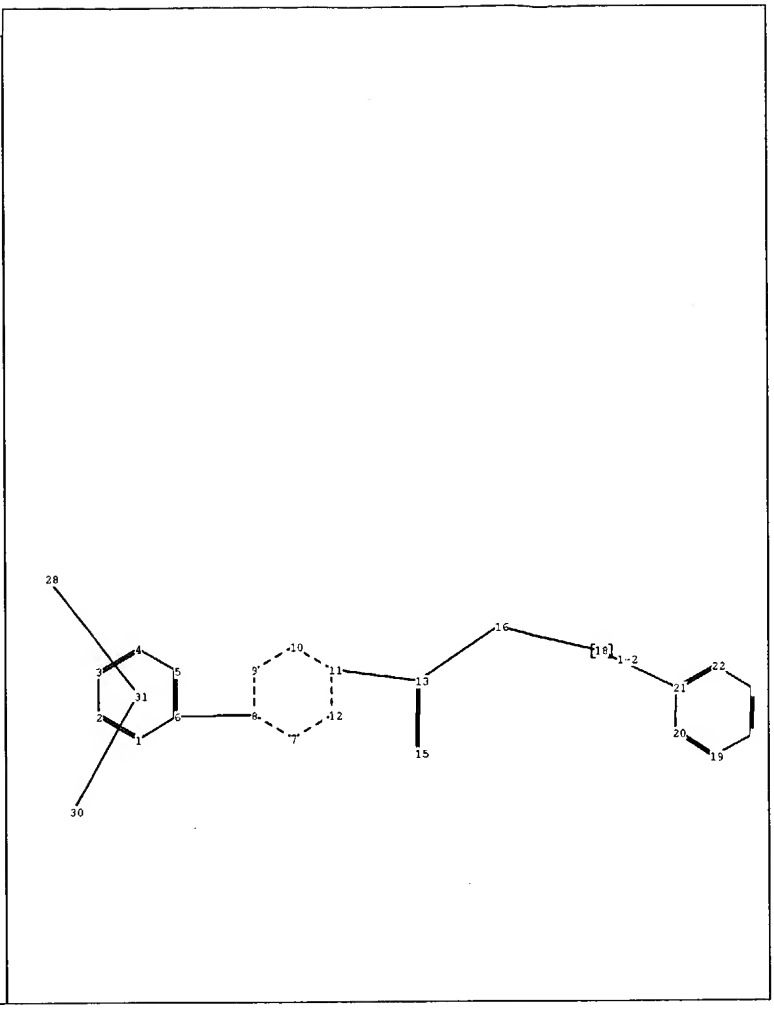

chain nodes :
13 15 16 18 28 30
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 19 20 21 22 23 24
chain bonds :
6-8 11-13 13-15 13-16 16-18 18-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 19-20 19-24 20-21
21-22 22-23 23-24
exact/norm bonds :
7-8 7-12 8-9 9-10 10-11 11-12 11-13 13-15 13-16 16-18
exact bonds :
6-8 18-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24
isolated ring systems :
containing 1 : 7 : 19 :

G1:O,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 15:CLASS 16:CLASS 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom
23:Atom 24:Atom 28:CLASS 29:CLASS 30:CLASS 31:CLASS

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
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NEWS 4	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 5	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 6	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
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NEWS 8	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
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NEWS 10	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
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NEWS 12	SEP 14	STN Patent Forum to be held October 13, 2004, in Iselin, NJ
NEWS 13	SEP 27	STANDARDS will no longer be available on STN
NEWS 14	SEP 27	SWETSCAN will no longer be available on STN

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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NEWS LOGIN	Welcome Banner and News Items
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FILE 'HOME' ENTERED AT 16:50:16 ON 29 SEP 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:50:55 ON 29 SEP 2004
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STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

h eb c g cg b cg eb

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

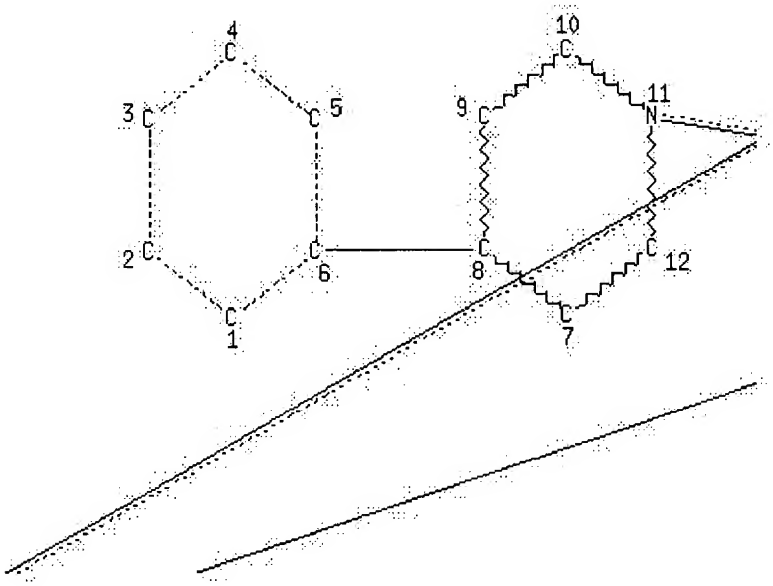
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

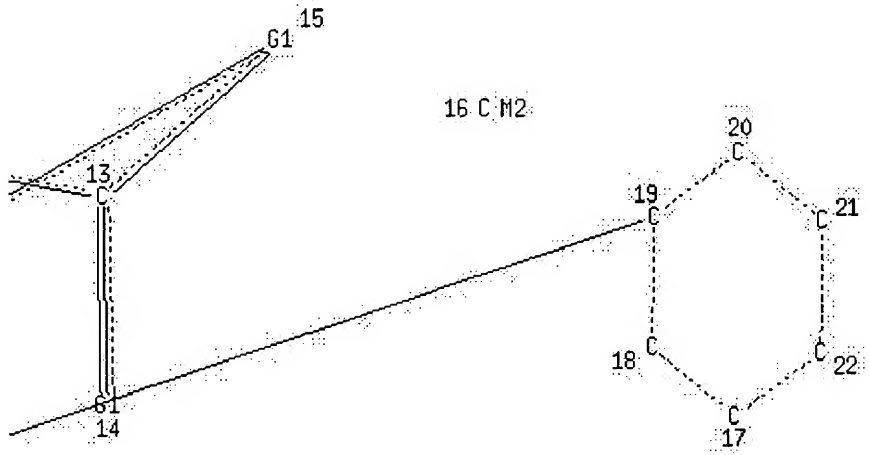
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR
0 24 S 25

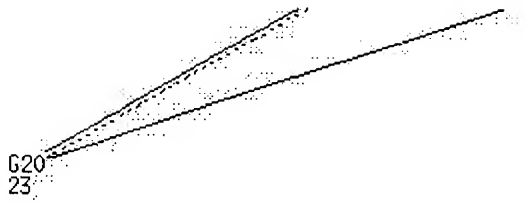


Page 1-A



Page 1-B

h eb c g cg b cg eb



Page 2-A
VAR G1=24/25
REP G20=(1-2) 16-15 16-19
NODE ATTRIBUTES:
HCOUNT IS M2 AT 16
NSPEC IS R AT 1
NSPEC IS R AT 2
NSPEC IS R AT 3
NSPEC IS R AT 4
NSPEC IS R AT 5
NSPEC IS R AT 6
NSPEC IS R AT 7
NSPEC IS R AT 8
NSPEC IS R AT 9
NSPEC IS R AT 10
NSPEC IS R AT 11
NSPEC IS R AT 12
NSPEC IS C AT 13
NSPEC IS C AT 14
NSPEC IS C AT 15
NSPEC IS C AT 16
NSPEC IS R AT 17
NSPEC IS R AT 18
NSPEC IS R AT 19
NSPEC IS R AT 20
NSPEC IS R AT 21
NSPEC IS R AT 22
NSPEC IS C AT 23
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 13 16 24 25
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

=> s l1
SAMPLE SEARCH INITIATED 16:53:49 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 981 TO ITERATE

100.0% PROCESSED 981 ITERATIONS 21 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 17741 TO 21499
PROJECTED ANSWERS: 145 TO 693

L2 21 SEA SSS SAM L1

h eb c g cg b cg eb

```
=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:53:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  20136 TO ITERATE

100.0% PROCESSED   20136 ITERATIONS                          358 ANSWERS
SEARCH TIME: 00.00.01

L3          358 SEA SSS FUL L1

=>
L4       STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4                STR
 0 27 S 28

                      X @24
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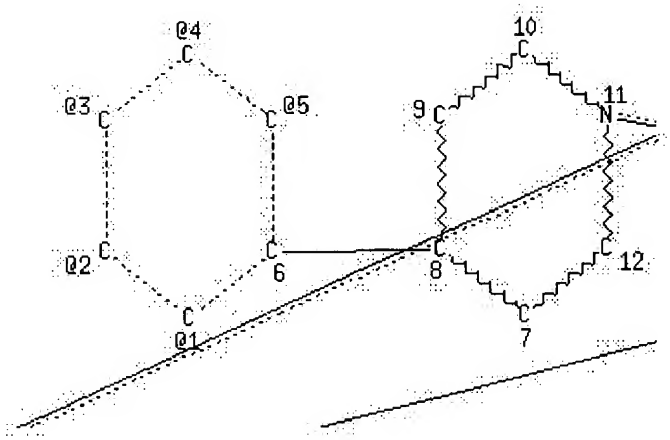
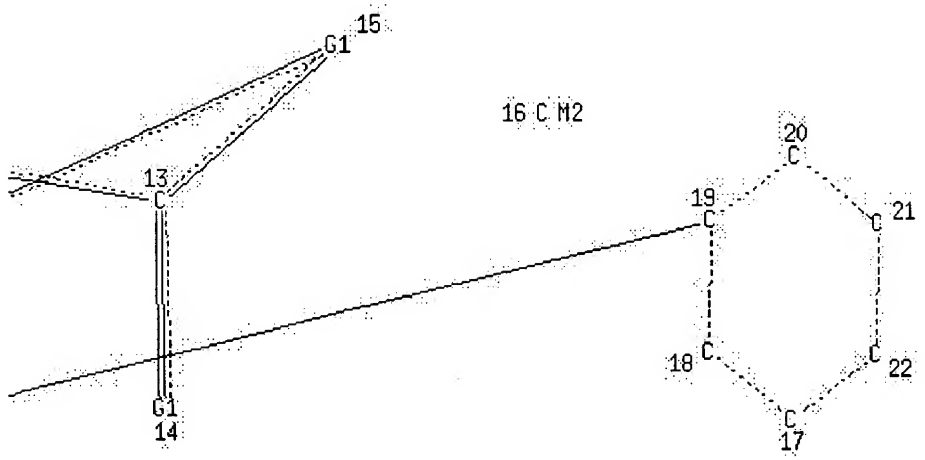
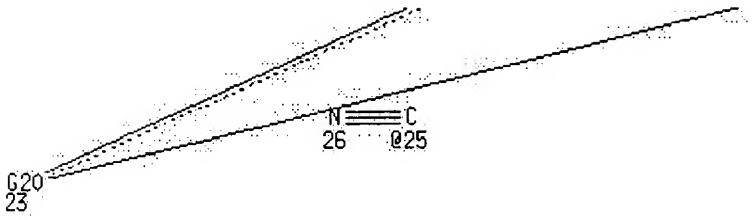


Page 1-A



Page 1-B

h eb c g cg b cg eb




```
Page 2-A
VAR G1=27/28
REP G20=(1-2) 16-15 16-19
VPA 24-1/2/3/4/5 S
VPA 25-1/2/3/4/5 S
NODE ATTRIBUTES:
HCOUNT  IS M2     AT  16
NSPEC   IS R      AT   1
NSPEC   IS R      AT   2
NSPEC   IS R      AT   3
NSPEC   IS R      AT   4
NSPEC   IS R      AT   5
NSPEC   IS R      AT   6
NSPEC   IS R      AT   7
NSPEC   IS R      AT   8
NSPEC   IS R      AT   9
NSPEC   IS R      AT  10
NSPEC   IS R      AT  11
NSPEC   IS R      AT  12
NSPEC   IS C      AT  13
NSPEC   IS C      AT  14
NSPEC   IS C      AT  15
NSPEC   IS C      AT  16
NSPEC   IS R      AT  17
NSPEC   IS R      AT  18
NSPEC   IS R      AT  19
NSPEC   IS R      AT  20
NSPEC   IS R      AT  21
NSPEC   IS R      AT  22
NSPEC   IS C      AT  23
NSPEC   IS C      AT  24
NSPEC   IS C      AT  25
NSPEC   IS C      AT  26
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  13 16 24 25 26 27 28
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE


=> s l4
SAMPLE SEARCH INITIATED 16:55:36 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     60 TO ITERATE

100.0% PROCESSED      60 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
```

h eb c g cg b cg eb

```
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          736 TO     1664
PROJECTED ANSWERS:               0 TO        0

L5             0 SEA SSS SAM L4

=> s l4 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:55:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   1205 TO ITERATE

100.0% PROCESSED    1205 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

L6             1 SEA SSS FUL L4

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   313.36     313.57

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FILE COVERS 1907 - 29 Sep 2004  VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004  (20040928/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l6
L7             1 L6

=> d l7, ibib abs fhitstr, 1

L7   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

```
ACCESSION NUMBER:         2000:379770  HCAPLUS
DOCUMENT NUMBER:          133:135208
TITLE:                    A versatile synthesis of 4-aryltetrahydropyridines via
                          palladium mediated Suzuki cross-coupling with cyclic
                          vinyl boronates
AUTHOR(S):                Eastwood, Paul R.
CORPORATE SOURCE:         Discovery Chemistry, Aventis Pharma, Essex, RM10 7XS,
```

h eb c g cg b cg eb

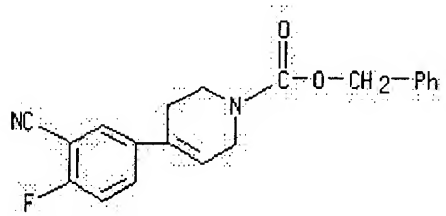
UK
SOURCE: Tetrahedron Letters (2000), 41(19), 3705-3708
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:135208

AB A simple prepn. of cyclic vinyl boronates derived from the vinyl triflates of N-protected tetrahydropyridines is described. Suzuki coupling of the boronates with aryl bromides, iodides, and triflates proceeds in good yield to give 4-aryltetrahydropyridines.

IT **286961-21-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of aryltetrahydropyridines via palladium mediated Suzuki cross-coupling with cyclic vinyl boronates)

RN 286961-21-5 HCAPLUS

CN 1(2H)-Pyridinecarboxylic acid, 4-(3-cyano-4-fluorophenyl)-3,6-dihydro-, phenylmethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.12	320.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.70	-0.70

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d his

h eb c g cg b cg eb

```
     (FILE 'HOME' ENTERED AT 16:50:16 ON 29 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 16:50:55 ON 29 SEP 2004
L1                STRUCTURE UPLOADED
L2             21 S L1
L3            358 S L1 FULL
L4                STRUCTURE UPLOADED
L5              0 S L4
L6              1 S L4 FULL

     FILE 'HCAPLUS' ENTERED AT 16:55:44 ON 29 SEP 2004
L7              1 S L6

     FILE 'CAOLD' ENTERED AT 16:56:09 ON 29 SEP 2004

=> s l6
L8              0 L6

=>
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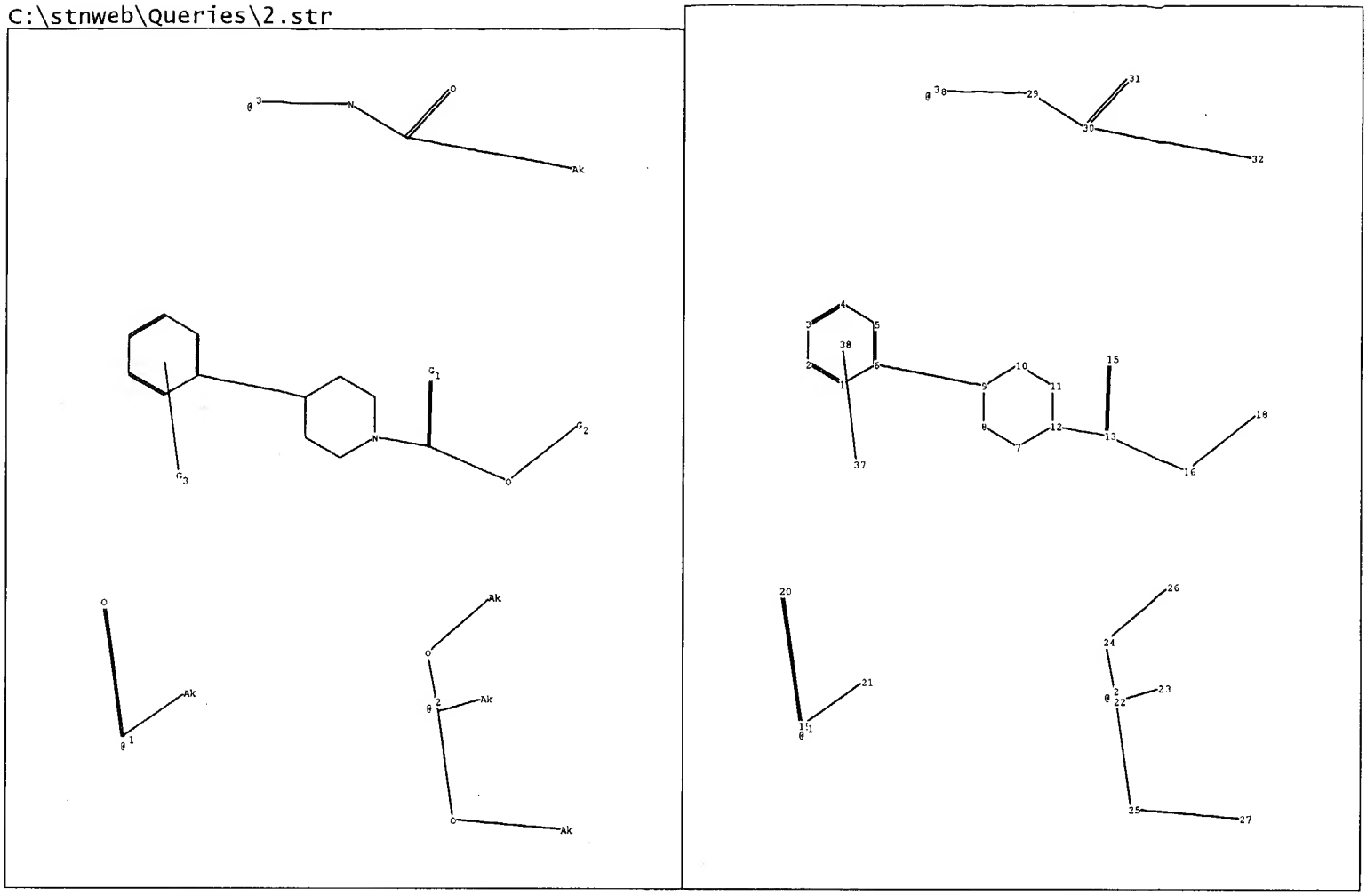

chain nodes :
13 15 16 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 37
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
6-9 12-13 13-15 13-16 16-18 19-20 19-21 22-23 22-24 22-25 24-26 25-27 28-29
29-30 30-31 30-32
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
7-8 7-12 8-9 9-10 10-11 11-12 12-13 13-15 13-16 16-18 19-20 19-21 22-23
22-24 22-25 24-26 25-27 28-29 29-30 30-31 30-32
exact bonds :
6-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 7 :

G1:O,S

G2:Ph,Ak

G3:CN,[*1],[*2],[*3]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 15:CLASS 16:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS
32:CLASS 37:CLASS 38:CLASS

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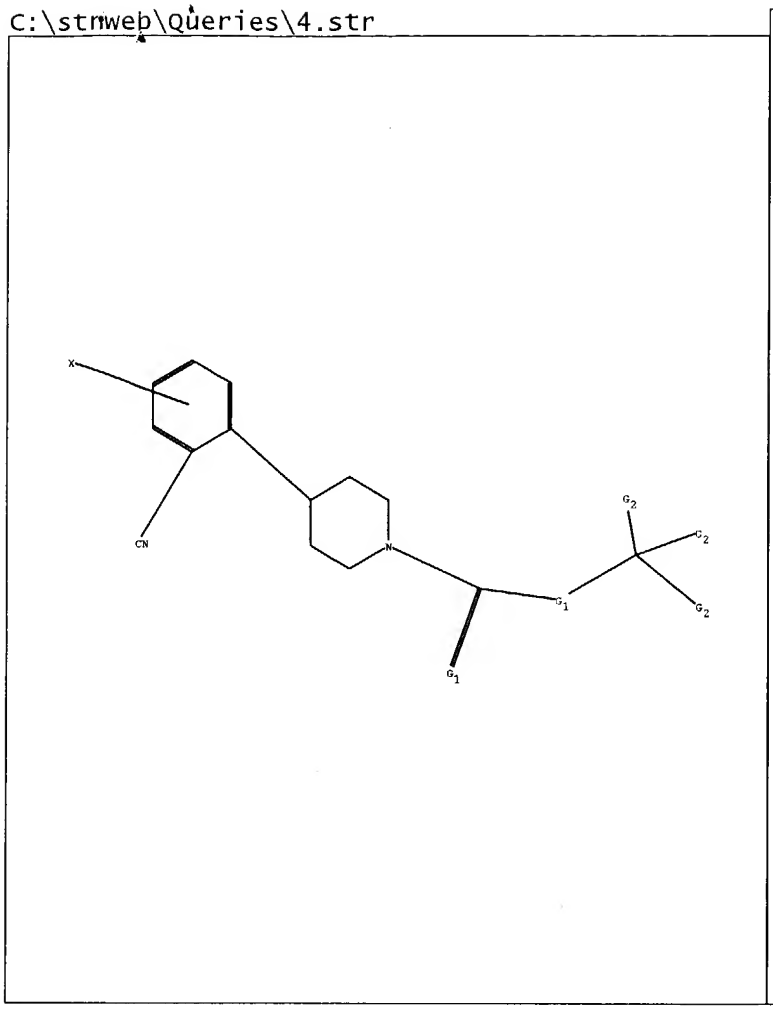

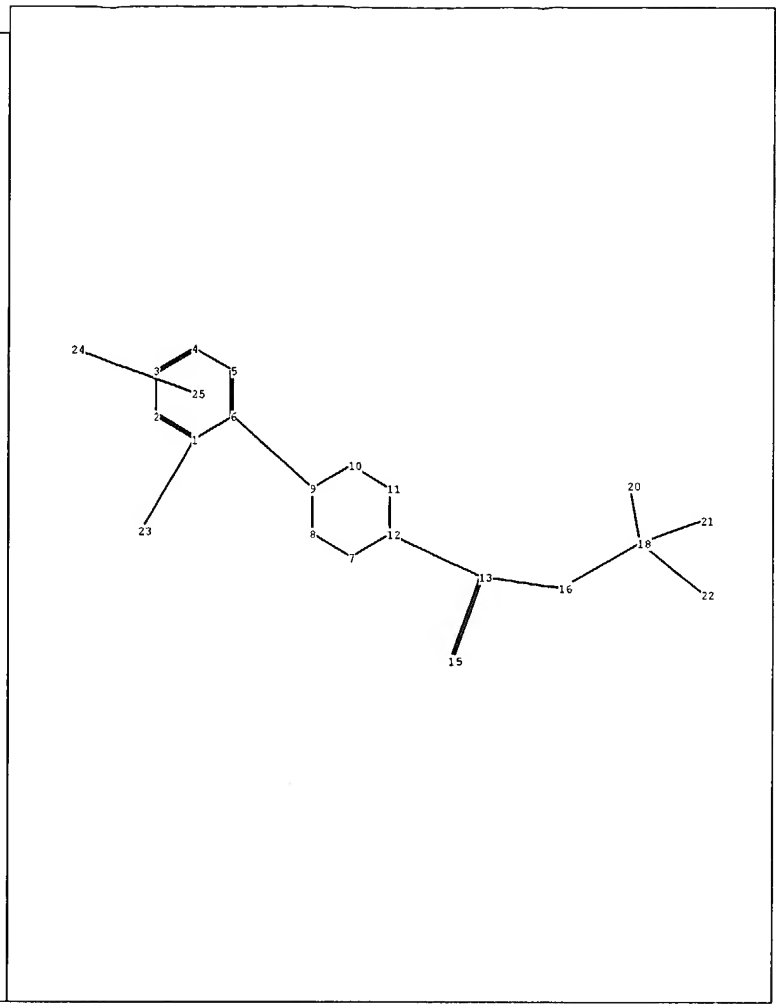

chain nodes :
13 15 16 18 20 21 22 23 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-23 6-9 12-13 13-15 13-16 16-18 18-22 18-20 18-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
7-8 7-12 8-9 9-10 10-11 11-12 12-13 13-15 13-16 16-18 18-22 18-20 18-21
exact bonds :
1-23 6-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 7 :

G1:O,S

G2:CH3,Et

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 15:CLASS 16:CLASS 18:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS
24:CLASS 25:CLASS

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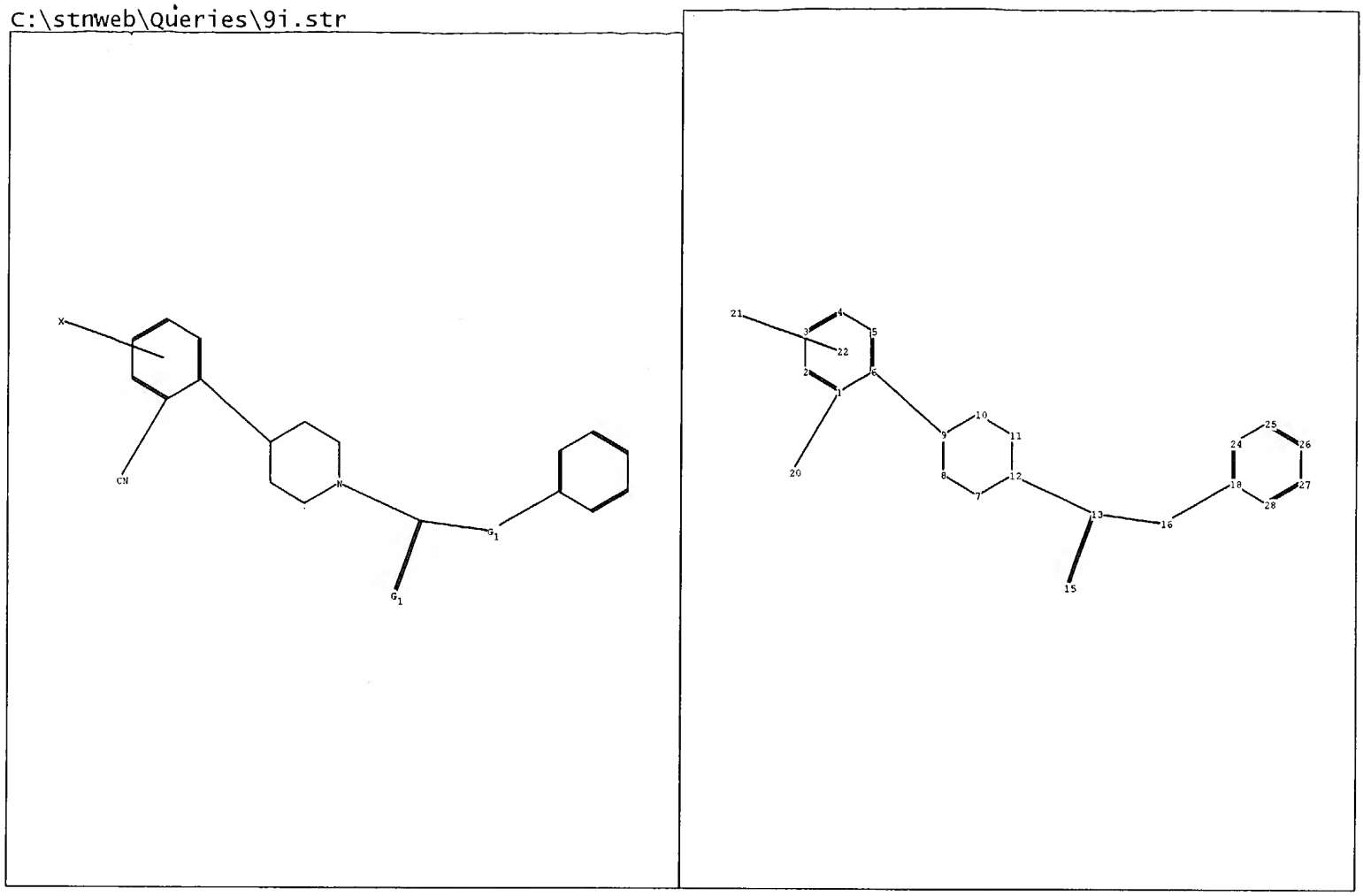

chain nodes :
13 15 16 20 21
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 18 24 25 26 27 28
chain bonds :
1-20 6-9 12-13 13-15 13-16 16-18
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 18-24 18-28 24-25
25-26 26-27 27-28
exact/norm bonds :
7-8 7-12 8-9 9-10 10-11 11-12 12-13 13-15 13-16 16-18
exact bonds :
1-20 6-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 18-24 18-28 24-25 25-26 26-27 27-28
isolated ring systems :
containing 1 : 7 :

G1:O,S

G2:CH3,Et

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 15:CLASS 16:CLASS 18:CLASS 20:CLASS 21:CLASS 22:CLASS 24:Atom
25:Atom 26:CLASS 27:Atom 28:Atom

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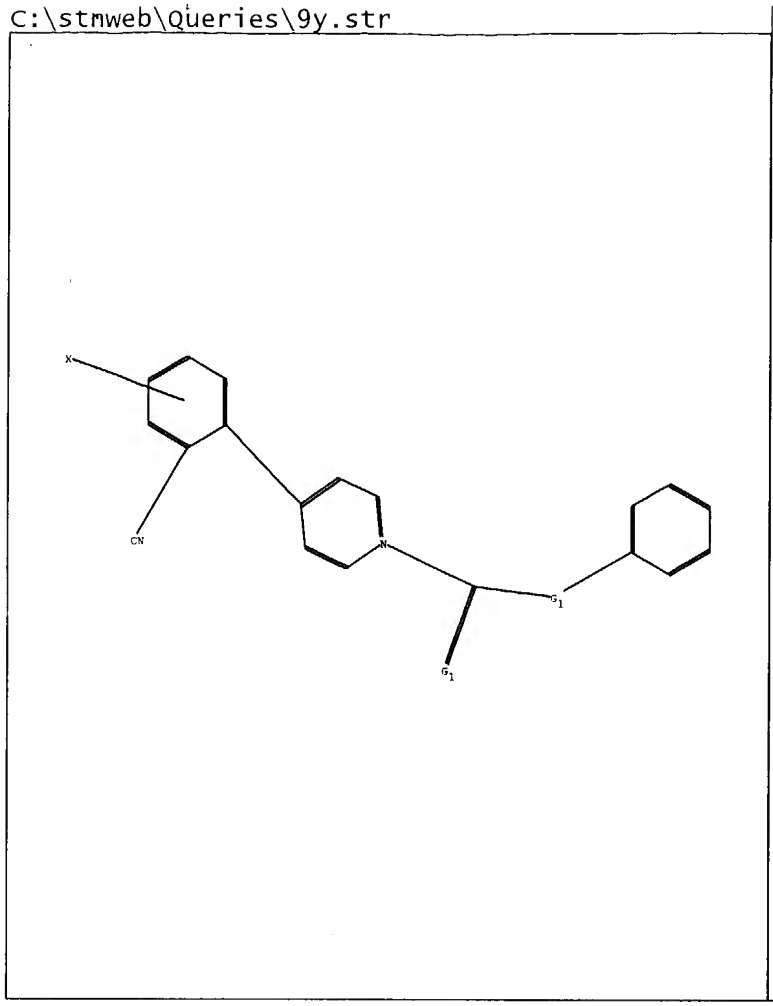

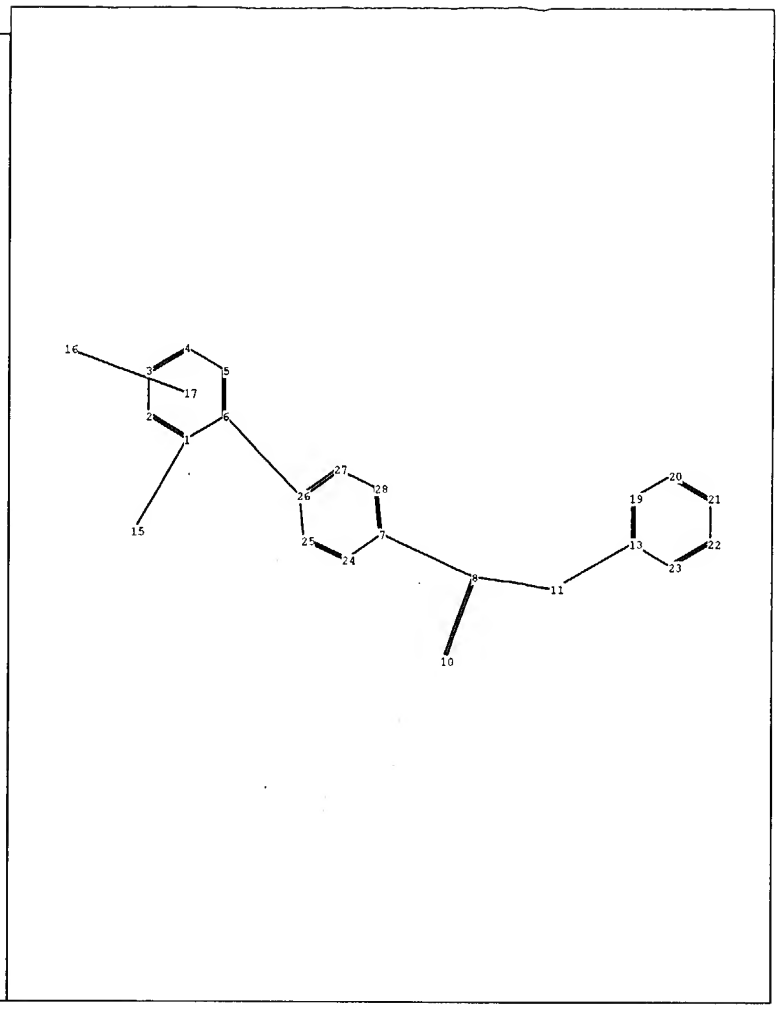

chain nodes :
8 10 11 15 16
ring nodes :
1 2 3 4 5 6 7 13 19 20 21 22 23 24 25 26 27 28
chain bonds :
1-15 6-26 7-8 8-10 8-11 11-13
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-24 7-28 13-19 13-23 19-20 20-21 21-22 22-23 24-25
25-26 26-27 27-28
exact/norm bonds :
7-8 8-10 8-11 11-13
exact bonds :
1-15 6-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-24 7-28 13-19 13-23 19-20 20-21 21-22 22-23 24-25
25-26 26-27 27-28
isolated ring systems :
containing 1 : 7 : 13 :

G1:O,S

G2:CH3,Et

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 10:CLASS 11:CLASS
13:CLASS 15:CLASS 16:CLASS 17:CLASS 19:Atom 20:Atom 21:CLASS 22:Atom 23:Atom
24:Atom 25:Atom 26:Atom 27:Atom 28:Atom

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jul 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 4	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 5	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 6	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 7	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 8	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 9	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 10	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
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NEWS 12	SEP 14	STN Patent Forum to be held October 13, 2004, in Iselin, NJ
NEWS 13	SEP 27	STANDARDS will no longer be available on STN
NEWS 14	SEP 27	SWETSCAN will no longer be available on STN

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:15:05 ON 29 SEP 2004

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'HCAPLUS' ENTERED AT 16:15:11 ON 29 SEP 2004
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FILE COVERS 1907 - 29 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004 (20040928/ED)

This file contains CAS Registry Numbers for easy and accurate
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=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.36	2.57

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STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L1 STRUCTURE UPLOADED

=> l1
L1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l1
L1 HAS NO ANSWERS
L1 STR

=> s l1
SAMPLE SEARCH INITIATED 16:17:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 28 TO ITERATE

100.0% PROCESSED 28 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

h eb c g cg b cg eb

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FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:          243 TO      877
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:17:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     548 TO ITERATE

100.0% PROCESSED     548 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.01

L3            3 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   156.68     159.25

FILE 'HCAPLUS' ENTERED AT 16:17:52 ON 29 SEP 2004
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FILE COVERS 1907 - 29 Sep 2004  VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004  (20040928/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L4            6 L3

=> s l4 and boice, g?/au
              7 BOICE, G?/AU
L5            1 L4 AND BOICE, G?/AU

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L5   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2004:511300  HCAPLUS
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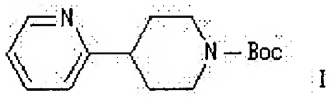
h eb c g cg b cg eb

DOCUMENT NUMBER: 141:174054
TITLE: Direct synthesis of 4-arylpiperidines via palladium/copper(I)-cocatalyzed Negishi coupling of a 4-piperidylzinc iodide with aromatic halides and triflates
AUTHOR(S): Corley, Edward G.; Conrad, Karen; Murry, Jerry A.; Savarin, Cecile; Holko, Justin; **Boice, Genevieve**
CORPORATE SOURCE: Departments of Process Research, and Chemical Engineering Research & Development, Merck Research Laboratories, Merck and Co., Inc., Rahway, NJ, 07065, USA
SOURCE: Journal of Organic Chemistry (2004), 69(15), 5120-5123
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

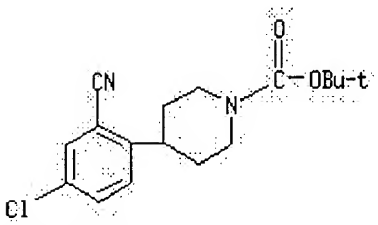


I

AB A general procedure for the synthesis of 4-arylpiperidines, e.g., I, via the coupling of 4-(N-Boc-piperidyl)zinc iodide with aryl halides and triflates is presented. The reaction required cocatalysis with both Cl2Pd(dppf) and a copper(I) species. An improved, safer procedure for the activation of zinc dust is also presented.

IT 732275-75-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-(Boc)-arylpiperidines via addn. of zinc to N-(Boc)-iodopiperidine followed by palladium/copper-catalzyed Negishi coupling with aryl halides and triflates)

RN 732275-75-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-chloro-2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'HCAPLUS' ENTERED AT 16:15:11 ON 29 SEP 2004

FILE 'REGISTRY' ENTERED AT 16:15:13 ON 29 SEP 2004
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 3 S L1 FULL

h eb c g cg b cg eb

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     FILE 'HCAPLUS' ENTERED AT 16:17:52 ON 29 SEP 2004
L4             6 S L3
L5             1 S L4 AND BOICE, G?/AU

=> s l4 not l5
L6             5 L4 NOT L5

=> s l6 and conrad, k?/au
           219 CONRAD, K?/AU
L7             0 L6 AND CONRAD, K?/AU

=> s l6 and corley, e?/au
            59 CORLEY, E?/AU
L8             0 L6 AND CORLEY, E?/AU

=> s l6 and matty, l?/au
            16 MATTY, L?/AU
L9             0 L6 AND MATTY, L?/AU

=> s l6 and murry, j?/au
            60 MURRY, J?/AU
L10            0 L6 AND MURRY, J?/AU

=> s l6 and savarin, c?/au
            14 SAVARIN, C?/AU
L11            0 L6 AND SAVARIN, C?/AU

=> d his

     (FILE 'HOME' ENTERED AT 16:15:05 ON 29 SEP 2004)

     FILE 'HCAPLUS' ENTERED AT 16:15:11 ON 29 SEP 2004

     FILE 'REGISTRY' ENTERED AT 16:15:13 ON 29 SEP 2004
L1               STRUCTURE UPLOADED
L2             0 S L1
L3             3 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 16:17:52 ON 29 SEP 2004
L4             6 S L3
L5             1 S L4 AND BOICE, G?/AU
L6             5 S L4 NOT L5
L7             0 S L6 AND CONRAD, K?/AU
L8             0 S L6 AND CORLEY, E?/AU
L9             0 S L6 AND MATTY, L?/AU
L10            0 S L6 AND MURRY, J?/AU
L11            0 S L6 AND SAVARIN, C?/AU

=> d l6, ibib abs fhitstr, 1-5

L6   ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2000:470758 HCAPLUS
DOCUMENT NUMBER: 133:187580
TITLE: In Vitro and in Vivo Evaluation of Dihydropyrimidinone C-5 Amides as Potent and Selective α1A Receptor Antagonists for the Treatment of Benign Prostatic Hyperplasia

h eb c g cg b cg eb

AUTHOR(S): Barrow, James C.; Nantermet, Philippe G.; Selnick, Harold G.; Glass, Kristen L.; Rittle, Kenneth E.; Gilbert, Kevin F.; Steele, Thomas G.; Homnick, Carl F.; Freidinger, Roger M.; Ransom, Rick W.; Kling, Paul; Reiss, Duane; Broten, Theodore P.; Schorn, Terry W.; Chang, Raymond S. L.; O'Malley, Stacey S.; Olah, Timothy V.; Ellis, Joan D.; Barrish, Andrea; Kassahun, Kelem; Leppert, Paula; Nagarathnam, Dhanapalan; Forray, Carlos

CORPORATE SOURCE: Departments of Medicinal Chemistry Pharmacology and Drug Metabolism, Merck Research Laboratories, West Point, PA, 19486, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(14), 2703-2718
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

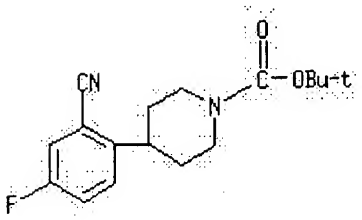
LANGUAGE: English

AB α1 Adrenergic receptors mediate both vascular and lower urinary tract tone, and α1 receptor antagonists such as terazosin are used to treat both hypertension and benign prostatic hyperplasia (BPH). Recently, three different subtypes of this receptor have been identified, with the α1A receptor being most prevalent in lower urinary tract tissue. This paper explores 4-aryldihydropyrimidinones attached to an aminopropyl-4-arylpiperidine via a C-5 amide as selective α1A receptor subtype antagonists. In receptor binding assays, these types of compds. generally display Ki values for the α1a receptor subtype of <1nM, while being greater than 100-fold selective vs. the α1b and α1d receptor subtypes. Many of these compds. were also evaluated in vivo and found to be more potent than terazosin in both a rat model of prostate tone and a dog model of intra-urethral pressure without significantly affecting blood pressure. While many of the compds. tested displayed poor pharmacokinetics, (4R)-4-(3,4-difluorophenyl)-6-methoxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid [3-[4-(4-fluorophenyl)piperidin-1-yl]propyl]amide (I) was found to have adequate bioavailability (>20%) and half-life (>6 h) in both rats and dogs. Due to its selectivity for the α1a over the α1b and α1d receptors, as well as its favorable pharmacokinetic profile, I has the potential to relieve the symptoms of BPH without eliciting effects on the cardiovascular system.

IT **256951-76-5P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and properties and reactions of; prepn. of dihydropyrimidinone C-5 amides as potent and selective α1A receptor antagonists for the treatment of benign prostatic hyperplasia in relation to)

RN 256951-76-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

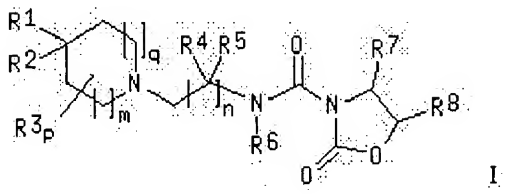
L6 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:335394 HCAPLUS
DOCUMENT NUMBER: 132:334452
TITLE: Preparation of oxazolidinones useful as α1-adrenoceptor antagonists
INVENTOR(S): Nerenberg, Jennie B.; Bock, Mark G.; Selnick, Harold G.; Payne, Linda
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000027827	A1	20000518	WO 1999-US26437		19991109
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6319932	B1	20011120	US 1999-438006		19991110
PRIORITY APPLN. INFO.:			US 1998-107839P	P	19981110
			US 1998-190506	A	19981112

OTHER SOURCE(S): MARPAT 132:334452
GI



I

AB Prepn. of oxazolidinones I [R1 = = (un)substituted Ph, naphthyl, heterocyclyl, etc.; R2 = H, CN, OH, etc.; R3 = alkyl; R4, R5 = H, alkyl, cycloalkyl; R6 = H, alkyl; R7 = (un)substituted Ph, pyridyl, thienyl, etc.; R8 = CONH2, CORc, etc.; m, q = 0-2; n = 1-3; p = 0-2], and their use as α1-adrenergic receptor antagonists, are described. One application of these compds. is in the treatment of benign prostatic hyperplasia. Another utility of I is provided by combination with a human 5-alpha reductase inhibitory compd., such that both acute and chronic relief from the effects of benign prostatic hyperplasia can be achieved. E.g., (4S,5R)-4-(3,4-difluorophenyl)-2-oxooxazolidine-3,5-dicarboxylic acid 5-amide 3-({3-[4-(4-fluorophenyl)piperidin-1-yl]propyl}amide) was prepd.

IT **256951-76-5P**

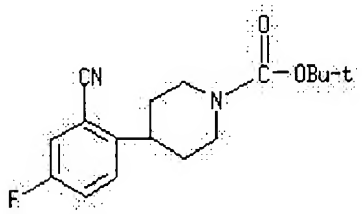
h eb c g cg b cg eb

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of oxazolidinones useful as α1-adrenoceptor antagonists)

RN 256951-76-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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L6 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:335386 HCAPLUS
DOCUMENT NUMBER: 132:334451
TITLE: Preparation of oxazolidin-2-one-3-carboxamides as α1A adrenoceptor antagonists
INVENTOR(S): Nerenberg, Jennie B.; Bock, Mark G.; Patane, Michael A.; Selnick, Harold G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000027817	A1	20000518	WO 1999-US26438		19991109
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6228870	B1	20010508	US 1999-437841		19991110
PRIORITY APPLN. INFO.:			US 1998-107838P	P	19981110
			US 1998-190505	A	19981112

OTHER SOURCE(S): MARPAT 132:334451
GI

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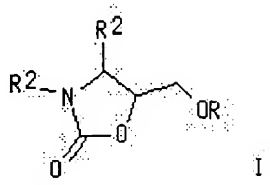

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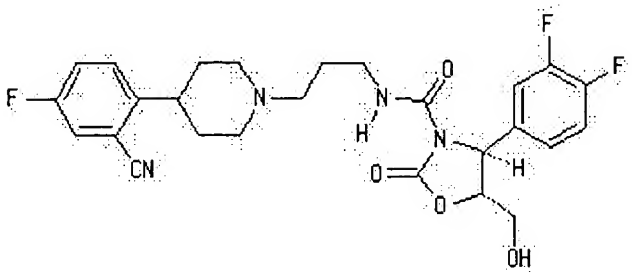


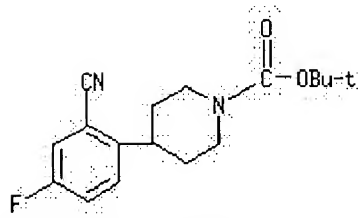
II

AB Title compds. [I; R = H, alkyl, Z1CF3; R1 = (un)substituted Ph; R2 = R3Z(CH2)nNHCO; R3 = (un)substituted Ph or -2-pyridyl; Z = 4-(un)substituted piperidine-4,1-diyl; Z1 = (CH2)1-4; n = 2-4] were prepd. Thus, (4S,5R)-I [R = THP, R1 = C6H3F2-3,4, R2 = CO2C6H4(NO2)-4] was amidated by 4,3-F(NC)C6H3Z(CH2)3NH2 (Z = piperidine-4,1-diyl)(prepn. each given) and the product deprotected to give title compd. II. Data for biol. activity of I were given.

IT **256951-76-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of oxazolidin-2-one-3-carboxamides as α1A adrenoceptor antagonists)

RN 256951-76-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:314542 HCAPLUS
DOCUMENT NUMBER: 132:308252
TITLE: Preparation of dihydropyridinones and pyrrolinones useful as alpha 1a adrenoceptor antagonists
INVENTOR(S): Barrow, James; Selnick, Harold G.; Nanterment, Philippe G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

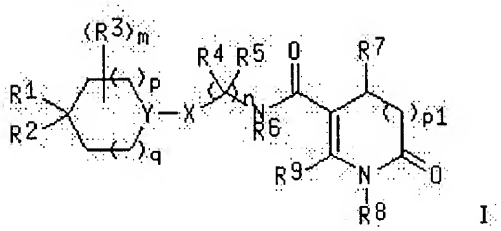
h eb c g cg b cg eb

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025782	A1	20000511	WO 1999-US24990	19991025
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6235759	B1	20010522	US 1999-428973	19991028
PRIORITY APPLN. INFO.:			US 1998-106095P	P 19981029
			US 1999-141463P	P 19990629

OTHER SOURCE(S): MARPAT 132:308252

GI



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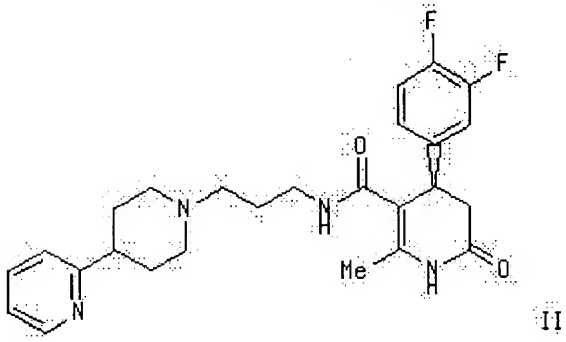


II

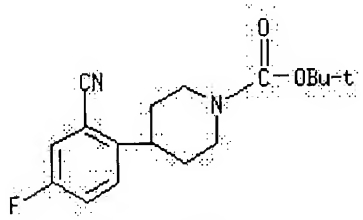
AB Novel dihydropyridinone and pyrrolinone compds. [I; Y = CH or N; X = CR4R5, when Y = N; X = NR6, when Y = CH; R1 = Ph, mono- or poly-substituted Ph, naphthyl, mono- or poly-substituted naphthyl, heterocyclic, or mono- or poly-substituted heterocyclic; wherein the heterocyclic is selected from the group consisting of pyridyl, pyrazinyl, thienyl, thiazolyl, furanyl and quinazolinyl; R2 = H, cyano, hydroxy, C1-6 alkoxy, CO2Rc, C(O)N(Rc)2, tetrazole, isooxadiazole, Ph, mono- or poly-substituted Ph, naphthyl, mono- or poly-substituted naphthyl, heterocyclic, or mono- or poly-substituted heterocyclic; wherein the heterocyclic is selected from the group consisting of pyridyl, thienyl and furanyl; R3 = a substituent connected to a ring atom other than CR1R2 or Y which is independently C1-4 alkyl; R4, R5 = H, C1-6 alkyl, C3-8 cycloalkyl; R6 = H, C1-4 alkyl; R7 = Ph, or mono- or poly-substituted phenyl; R8 = H, C1-6 alkyl, (CH2)0-4CO2Rc, (CH2)0-4C(O)Rc; R9 = H, halo, cyano, C1-6 alkyl, C3-8 cycloalkyl, C1-6 alkoxy, halogenated C1-6 alkyl, halogenated C3-8 cycloalkyl, halogenated C1-6 alkoxy, (CH2)1-4ORb, CO2Rc, C(O)Rc, or C(O)N(Rc)2; Rb, Rc = H, C1-6 alkyl, halogenated C1-6 alkyl; m =

h eb c g cg b cg eb

0-2; n = 2-4, when X = NR6; n = 1-3, when X = CR4R5; p1 = 0 or 1, provided that when Y = N, p1 = 0; p, q = 0-2, p+q≤3] or pharmaceutically acceptable salts thereof are prepd. Their use as alpha 1a adrenergic receptor antagonists is also described (no data). One application of these compds. is in the treatment of benign prostatic hyperplasia. These compds. are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compds. is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compds. is provided by combination with a human 5-alpha reductase inhibitory compd., such that both acute and chronic relief from the effects of benign prostatic hyperplasia can be achieved. Thus, 3-[4-(2-pyridyl)piperidin-1-yl]propylamine was condensed with (R)-(-)-4-(3,4-difluorophenyl)-6-methyl-3,4-dihydro-2-pyridinone-5-carboxylic using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 1-hydroxy-7-azabenenetriazole, and Et3N in DMF to give title compd. (II).

IT **256951-76-5P**, 4-(2-Cyano-4-fluorophenyl)piperidine-1-carboxylic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of dihydropyridinones and pyrrolinones useful as alpha 1a adrenoceptor antagonists for treatment of benign prostatic hyperplasia)

RN 256951-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Other References

ACCESSION NUMBER: 2000:98550 HCAPLUS
DOCUMENT NUMBER: 132:137405
TITLE: 2-Oxo-N-(3-piperidinylpropyl)tetrahydropyrimidine-5-carboxamide derivatives as α1a adrenergic receptor antagonists
INVENTOR(S): Barrow, James C.; Nantermet, Philippe G.; Selnick, Harold G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006565	A1	20000210	WO 1999-US16998	19990727

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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US 6339090	B1	20020115	US 1999-363631		19990729
PRIORITY APPLN. INFO.:			US 1998-94600P	P	19980730
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OTHER SOURCE(S): MARPAT 132:137405
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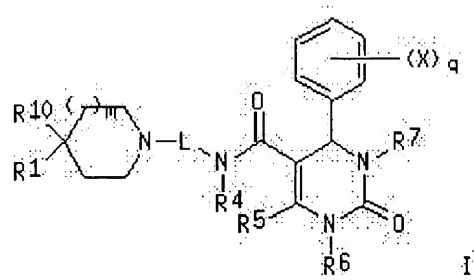

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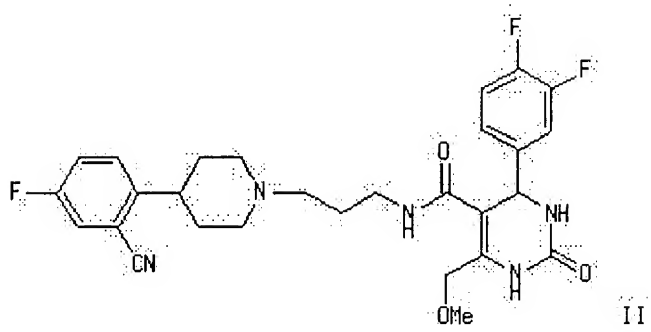

II

AB Title compds. (I) [wherein R1 = (un)substituted Ph or pyridyl; R2 = (cyclo)alkyl or trifluoromethyl(alkyl); R4 = H, alkyl, or trifluoromethyl(alkyl); R5 = H, (alkoxy)alkyl, or trifluoromethyl(alkyl); R6 = H or alkyl; R7 = H, (alkoxy)alkyl, alkoxycarbonyl, acyl, or trifluoromethyl(alkyl); R8 and R9 = independently (cyclo)alkyl or trifluoromethyl(alkyl); R10 = H, OH, CN, alkyl, alkoxy(alkyl), or trifluoromethyl(alkyl); L = (CH2)n, (CHR2)n, CR8R9(CH2)n-1, (CH2)n-1R8R9, CH2CR8R9CH2, CH2CH2CR8R9CH2, or CH2CR8R9CH2CH2; X = independently halo, CN, or alkyl; m = 0-2; n = 2-4; q = 0-4] were prepd. for use in the treatment of benign prostatic hyperplasia. Over fifty target compds. were synthesized and tested for α1a adrenergic receptor binding and selectivity. For example, 4-(R)-(3,4-difluorophenyl)-6-methoxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid was amidated with 2-[1-(3-aminopropyl)piperidin-4-yl]-5-fluorobenzonitrile.2HCl (prepn. given) in the presence of TEA, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide.HCl, and 1-hydroxybenzotriazole.H2O in DMF to yield (4R)-II. All tested compds. bound to transfected human α1a cell line (ATCC CRL 11140) with Ki ≤ 30 nM and were at least 10 fold more selective in binding to α1a receptors vs. binding to α1b or α1d

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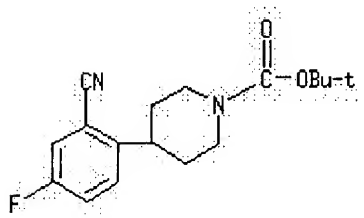
receptors. Thus, these compds. are selective in their ability to relax smooth muscle tissue enriched in the α1a receptor subtype without at the same time inducing hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the invention compds. is to provide acute relief to males suffering from benign prostatic hyperplasia by permitting less hindered urine flow. These compds. may also be used in combination with a human 5α reductase inhibitory compd., such as finasteride, to provide both acute and chronic relief from the effects of benign prostatic hyperplasia.

IT **256951-76-5P**, 4-(2-Cyano-4-fluorophenyl)piperidine-1-carboxylic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of 2-oxo-N-(3-piperidinylpropyl)tetrahydropyrimidine-5-carboxamide derivs. as α1a adrenergic receptor antagonists for the treatment of benign prostatic hyperplasia)

RN 256951-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'HCAPLUS' ENTERED AT 16:15:11 ON 29 SEP 2004

FILE 'REGISTRY' ENTERED AT 16:15:13 ON 29 SEP 2004
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L2 0 S L1
L3 3 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 16:17:52 ON 29 SEP 2004
L4 6 S L3
L5 1 S L4 AND BOICE, G?/AU
L6 5 S L4 NOT L5
L7 0 S L6 AND CONRAD, K?/AU
L8 0 S L6 AND CORLEY, E?/AU
L9 0 S L6 AND MATTY, L?/AU
L10 0 S L6 AND MURRY, J?/AU
L11 0 S L6 AND SAVARIN, C?/AU

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	33.28	192.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

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FILE LAST UPDATED:  01 May 1997 (19970501/UP)

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     (FILE 'HOME' ENTERED AT 16:15:05 ON 29 SEP 2004)

     FILE 'HCAPLUS' ENTERED AT 16:15:11 ON 29 SEP 2004

     FILE 'REGISTRY' ENTERED AT 16:15:13 ON 29 SEP 2004
L1              STRUCTURE UPLOADED
L2            0 S L1
L3            3 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 16:17:52 ON 29 SEP 2004
L4            6 S L3
L5            1 S L4 AND BOICE, G?/AU
L6            5 S L4 NOT L5
L7            0 S L6 AND CONRAD, K?/AU
L8            0 S L6 AND CORLEY, E?/AU
L9            0 S L6 AND MATTY, L?/AU
L10           0 S L6 AND MURRY, J?/AU
L11           0 S L6 AND SAVARIN, C?/AU

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STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

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L13 STRUCTURE UPLOADED

=> l13
L13 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

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L13 HAS NO ANSWERS
L13 STR

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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 0 TO 0

L14 0 SEA SSS SAM L13

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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 0 TO 0

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FULL SCREEN SEARCH COMPLETED -      94 TO ITERATE

100.0% PROCESSED       94 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

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L17 HAS NO ANSWERS
L17              STR

=> s l17
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                        BATCH    **COMPLETE**
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L18            0 SEA SSS SAM L17

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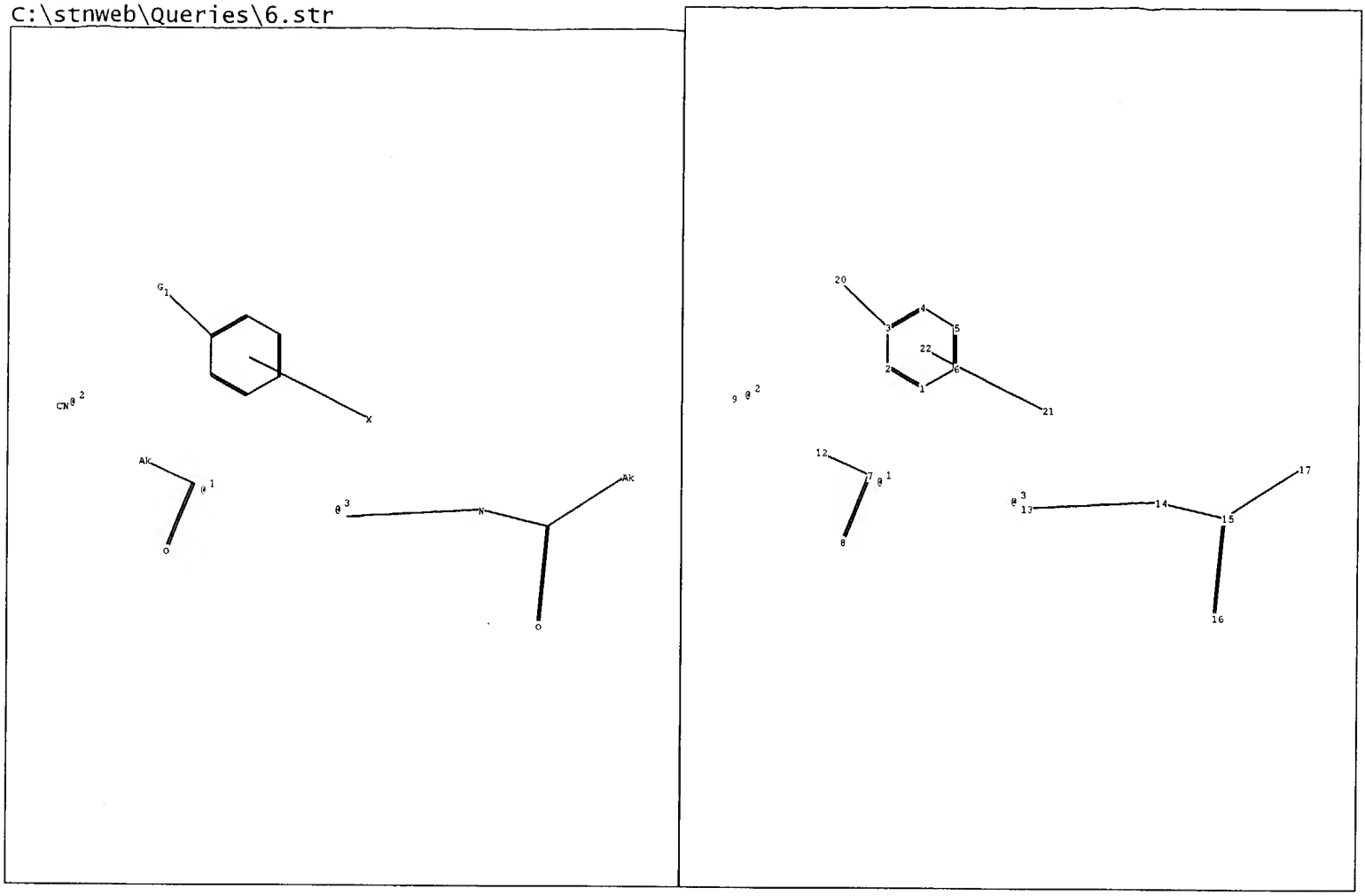

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ring nodes :
1 2 3 4 5 6
chain bonds :
3-20 7-8 7-12 13-14 14-15 15-16 15-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
3-20 7-8 7-12 13-14 14-15 15-16 15-17
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:[*1],[*2],[*3]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 12:CLASS
13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 20:CLASS 21:CLASS 22:CLASS

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                     resulting in a closer connection to BABS
  NEWS  4  AUG 02    IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                     fields
  NEWS  5  AUG 02    CAplus and CA patent records enhanced with European and Japan
                     Patent Office Classifications
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  NEWS  9  SEP 01    INPADOC: New family current-awareness alert (SDI) available
  NEWS 10  SEP 01    New pricing for the Save Answers for SciFinder Wizard within
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  NEWS 11  SEP 01    New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
  NEWS 12  SEP 14    STN Patent Forum to be held October 13, 2004, in Iselin, NJ
  NEWS 13  SEP 27    STANDARDS will no longer be available on STN
  NEWS 14  SEP 27    SWETSCAN will no longer be available on STN

  NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
                MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
                AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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STRUCTURE FILE UPDATES:   28 SEP 2004  HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES:  28 SEP 2004  HIGHEST RN 753424-73-6
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TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

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http://www.cas.org/ONLINE/DBSS/registryss.html

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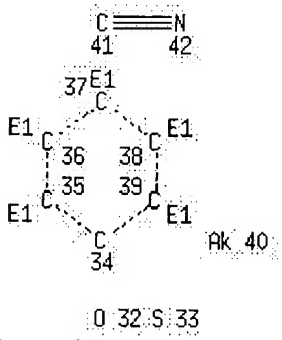

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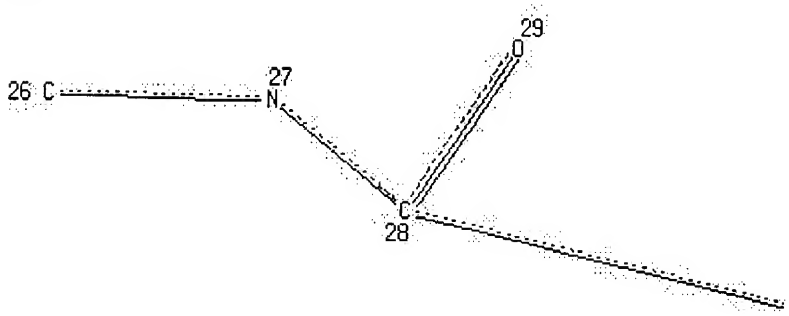

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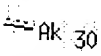

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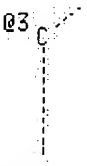

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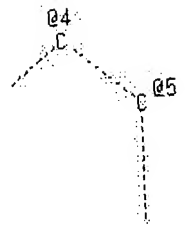

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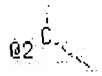

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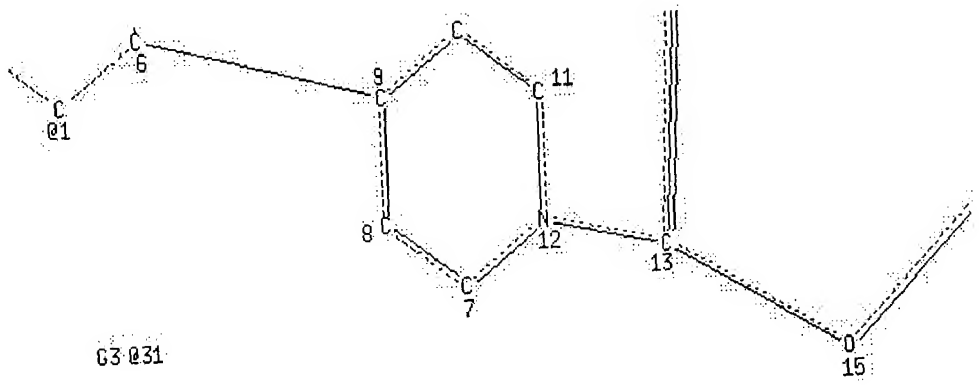

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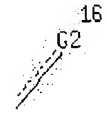

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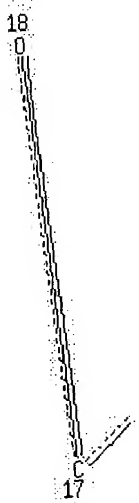

Page 4-A

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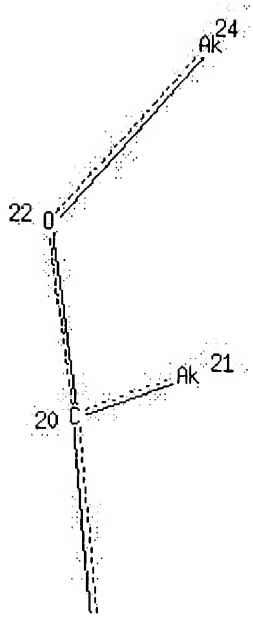
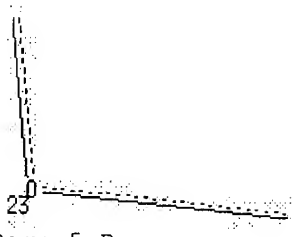


Page 4-B



Page 5-B

Ak 25

Page 5-C

VAR G1=32/33
VAR G2=34/40
VAR G3=41/17/20/26
VPA 31-1/2/3/4/5 S
NODE ATTRIBUTES:

HCOUNT	IS E1	AT	35
HCOUNT	IS E1	AT	36
HCOUNT	IS E1	AT	37
HCOUNT	IS E1	AT	38
HCOUNT	IS E1	AT	39
NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS R	AT	6
NSPEC	IS R	AT	7
NSPEC	IS R	AT	8
NSPEC	IS R	AT	9
NSPEC	IS R	AT	10
NSPEC	IS R	AT	11
NSPEC	IS R	AT	12
NSPEC	IS C	AT	13
NSPEC	IS C	AT	14
NSPEC	IS C	AT	15
NSPEC	IS C	AT	16
NSPEC	IS C	AT	17

h eb c g cg b cg eb

```
NSPEC   IS C      AT  18
NSPEC   IS C      AT  19
NSPEC   IS C      AT  20
NSPEC   IS C      AT  21
NSPEC   IS C      AT  22
NSPEC   IS C      AT  23
NSPEC   IS C      AT  24
NSPEC   IS C      AT  25
NSPEC   IS C      AT  26
NSPEC   IS C      AT  27
NSPEC   IS C      AT  28
NSPEC   IS C      AT  29
NSPEC   IS C      AT  30
NSPEC   IS C      AT  31
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  13 15 17 18 19 20 21 22 23 24 25 26 27 28 29 30 32
          33 34 35 36 37 38 39 40 41 42
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  42

STEREO ATTRIBUTES: NONE


=> s l1
SAMPLE SEARCH INITIATED 15:21:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    420 TO ITERATE

100.0% PROCESSED     420 ITERATIONS                              1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         7171 TO     9629
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 15:21:38 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   8739 TO ITERATE

100.0% PROCESSED    8739 ITERATIONS                             24 ANSWERS
SEARCH TIME: 00.00.01

L3           24 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             160.46     160.67

FILE 'HCAPLUS' ENTERED AT 15:28:58 ON 29 SEP 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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h eb c g cg b cg eb

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FILE COVERS 1907 - 29 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004 (20040928/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3/thu
22 L3
622869 THU/RL
L4 1 L3/THU
(L3 (L) THU/RL)

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.36	163.03

FILE 'REGISTRY' ENTERED AT 15:29:06 ON 29 SEP 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s l3/prep
'PREP' IS NOT A VALID CROSSOVER QUALIFIER FOR L3
Answer sets created in a different file may be field qualified with a limited set of qualifiers. Enter HELP CROSSOVER at an arrow prompt (=>) for specific information.

=> file hcaplus

h eb c g cg b cg eb

```
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY     SESSION
FULL ESTIMATED COST                                         0.42     163.45

FILE 'HCAPLUS' ENTERED AT 15:29:32 ON 29 SEP 2004
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```
FILE COVERS 1907 - 29 Sep 2004  VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004  (20040928/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d his

     (FILE 'HOME' ENTERED AT 15:21:00 ON 29 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 15:21:10 ON 29 SEP 2004
L1              STRUCTURE UPLOADED
L2            1 S L1
L3           24 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 15:28:58 ON 29 SEP 2004
L4            1 S L3/THU

     FILE 'REGISTRY' ENTERED AT 15:29:06 ON 29 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 15:29:32 ON 29 SEP 2004

=> s l3/prep
            22 L3
       3202496 PREP/RL
L5          22 L3/PREP
                (L3 (L) PREP/RL)

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY     SESSION
FULL ESTIMATED COST                                         9.44     172.89

FILE 'REGISTRY' ENTERED AT 15:31:56 ON 29 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
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h eb c g cg b cg eb

provided by InfoChem.

STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L6 STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6 STR

=> s l6 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 15:42:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - >1,000,000 TO ITERATE

< 1.4% PROCESSED 90882 ITERATIONS 2162 ANSWERS

< 2.7% PROCESSED 171514 ITERATIONS 3829 ANSWERS

< 5.2% PROCESSED 334046 ITERATIONS 7431 ANSWERS

< 6.0% PROCESSED 383092 ITERATIONS 8206 ANSWERS

< 6.3% PROCESSED 400000 ITERATIONS 8381 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.01.15

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: EXCEEDS 1000000
PROJECTED ANSWERS: EXCEEDS 132541

L7 8381 SEA SSS FUL L6

=> file hcaplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	164.66	337.55

FILE 'HCAPLUS' ENTERED AT 15:45:57 ON 29 SEP 2004
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h eb c g cg b cg eb

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FILE COVERS 1907 - 29 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004 (20040928/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d his

(FILE 'HOME' ENTERED AT 15:21:00 ON 29 SEP 2004)

FILE 'REGISTRY' ENTERED AT 15:21:10 ON 29 SEP 2004
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 24 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 15:28:58 ON 29 SEP 2004
L4 1 S L3/THU

FILE 'REGISTRY' ENTERED AT 15:29:06 ON 29 SEP 2004

FILE 'HCAPLUS' ENTERED AT 15:29:32 ON 29 SEP 2004
L5 22 S L3/PREP

FILE 'REGISTRY' ENTERED AT 15:31:56 ON 29 SEP 2004
L6 STRUCTURE UPLOADED
L7 8381 S L6 FULL

FILE 'HCAPLUS' ENTERED AT 15:45:57 ON 29 SEP 2004

=> s l5 and boice, g?/au
7 BOICE, G?/AU
L8 1 L5 AND BOICE, G?/AU

=> d l8, ibib abs hitstr, 1

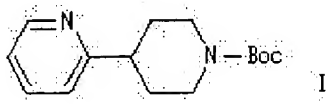
L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:511300 HCAPLUS
DOCUMENT NUMBER: 141:174054
TITLE: Direct synthesis of 4-arylpiperidines via palladium/copper(I)-cocatalyzed Negishi coupling of a 4-piperidylzinc iodide with aromatic halides and triflates
AUTHOR(S): Corley, Edward G.; Conrad, Karen; Murry, Jerry A.; Savarin, Cecile; Holko, Justin; **Boice, Genevieve**
CORPORATE SOURCE: Departments of Process Research, and Chemical Engineering Research & Development, Merck Research Laboratories, Merck and Co., Inc., Rahway, NJ, 07065,

h eb c g cg b cg eb

USA
SOURCE: Journal of Organic Chemistry (2004), 69(15), 5120-5123
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

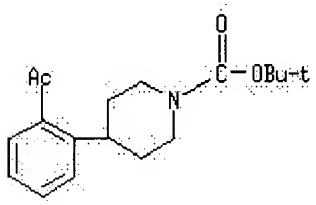


I

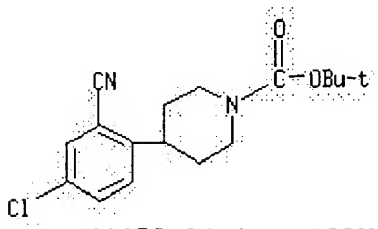
AB A general procedure for the synthesis of 4-arylpiperidines, e.g., I, via the coupling of 4-(N-Boc-piperidyl)zinc iodide with aryl halides and triflates is presented. The reaction required cocatalysis with both Cl2Pd(dppf) and a copper(I) species. An improved, safer procedure for the activation of zinc dust is also presented.

IT **255050-91-0P 732275-75-1P 732275-94-4P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of N-(Boc)-arylpiperidines via addn. of zinc to N-(Boc)-iodopiperidine followed by palladium/copper-catalzyed Negishi coupling with aryl halides and triflates)

RN 255050-91-0 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-acetylphenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

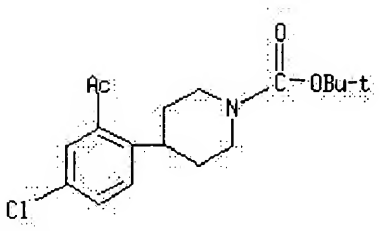


RN 732275-75-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-chloro-2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 732275-94-4 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-acetyl-4-chlorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

h eb c g cg b cg eb



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his

     (FILE 'HOME' ENTERED AT 15:21:00 ON 29 SEP 2004)

     FILE 'REGISTRY' ENTERED AT 15:21:10 ON 29 SEP 2004
L1             STRUCTURE UPLOADED
L2           1 S L1
L3          24 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 15:28:58 ON 29 SEP 2004
L4           1 S L3/THU

     FILE 'REGISTRY' ENTERED AT 15:29:06 ON 29 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 15:29:32 ON 29 SEP 2004
L5          22 S L3/PREP

     FILE 'REGISTRY' ENTERED AT 15:31:56 ON 29 SEP 2004
L6             STRUCTURE UPLOADED
L7         8381 S L6 FULL

     FILE 'HCAPLUS' ENTERED AT 15:45:57 ON 29 SEP 2004
L8           1 S L5 AND BOICE, G?/AU

=> s l5 not l8
L9          21 L5 NOT L8

=> s l9 and conrad, k?/au
          219 CONRAD, K?/AU
L10         0 L9 AND CONRAD, K?/AU

=> s l9 and corley, e?/au
           59 CORLEY, E?/AU
L11         0 L9 AND CORLEY, E?/AU

=> s l9 and matty, l?/au
           16 MATTY, L?/AU
L12         0 L9 AND MATTY, L?/AU

=> s l9 and murry, j?/au
           60 MURRY, J?/AU
L13         0 L9 AND MURRY, J?/AU

=> s l9 and savarin, c?/au
           14 SAVARIN, C?/AU
L14         0 L9 AND SAVARIN, C?/AU

=> d l9, ibib abs hitstr, 1-21
```

h eb c g cg b cg eb

L9 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

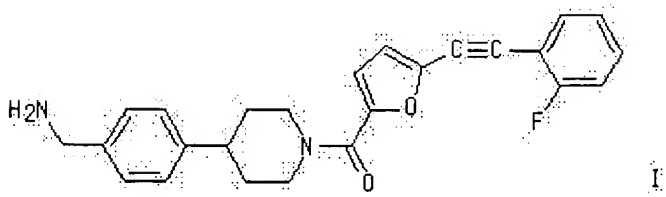
Full Text | Citing References

ACCESSION NUMBER: 2004:589545 HCAPLUS
DOCUMENT NUMBER: 141:140322
TITLE: Preparation of [4-(3-aminomethylphenyl)piperidin-1-yl][5-(2-fluorophenylethynyl)furan-2-yl]methanone as inhibitor of mast cell tryptase
INVENTOR(S): Pauls, Heinz W.; Aldous, Suzanne C.; Merriman, Gregory H.; Farr, Robert A.; Sledeski, Adam W.
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060884	A1	20040722	WO 2003-US40653	20031218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-436534P P 20021226
GI



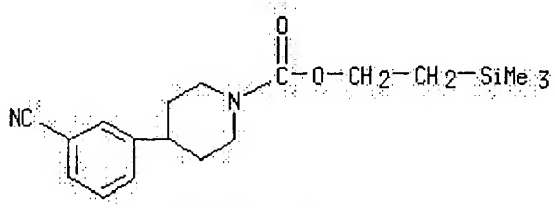
I

AB Title compds. of formula I, and a prodrug, its pharmaceutically acceptable trifluoroacetate or methanesulfonate salts or solvates thereof, was prepd. as an inhibitor of mast cell tryptase. For example, I was given in a multiple-step synthesis starting from 4-oxopiperidine-1-carboxylic 2-(trimethylsilanyl)ethyl ester. I showed inhibition of β-tryptase with Ki value of 7.6 nM. Thus, I and its pharmaceutical compns. are useful as an inhibitor of tryptase.

IT **725228-57-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of [4-(3-aminomethylphenyl)piperidin-1-yl][5-(2-fluorophenylethynyl)furan-2-yl]methanone as inhibitor of mast cell Tryptase)

RN 725228-57-9 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(3-cyanophenyl)-, 2-(trimethylsilyl)ethyl ester (9CI) (CA INDEX NAME)

h eb c g cg b cg eb



L9 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

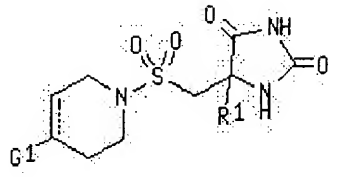
ACCESSION NUMBER: 2004:252505 HCAPLUS
DOCUMENT NUMBER: 140:287387
TITLE: Preparation of imidazolidinedione derivatives and their use as metalloproteinase inhibitors
INVENTOR(S): Chapman, David; Eriksson, Anders; Kristoffersson, Anna; Shamovsky, Igor; Stenvall, Kristina
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024718	A1	20040325	WO 2003-SE1407	20030910

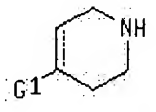
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2002-2693 A 20020911
OTHER SOURCE(S): CASREACT 140:287387; MARPAT 140:287387
GI

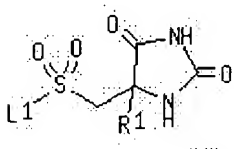
h eb c g cg b cg eb



I



II



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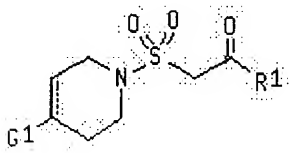


IV

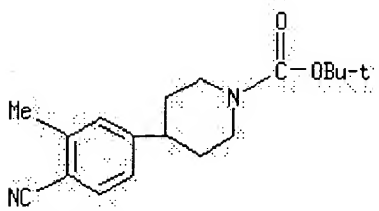
AB The invention provides compds. I [R1 = H, C1-6-alkyl, (un)satd. (un)substituted 3- to 10-membered ring {optionally contg. a heteroatom - N, O, S; optionally substituted with halogen, OH, CN, CO2H, NR2R3, CONR4R5, C1-6-alkyl, C1-6-alkoxy, C1-6-alkylcarbonyloxy, S(O)m-(C1-6-alkyl), C1-6-alkyl-sulfonylamino, OCH2Ph}; R2, R3, R4, R5 = H, C1-6-alkyl, C1-6-hydroxyalkyl, C1-6-haloalkyl, (C1-6-alkoxy)-C1-6-alkyl; m = 0, 1, 2; G1 = 5- or 6-membered aryl, heteroaryl monocyclic ring , optionally fused to form a 8- to 10-membered ring and optionally substituted with halogen, OH, CN, NO2, (un)substituted C1-6-alkyl, C2-6-alkenyl, C1-6-alkoxy, C1-6-haloalkoxy, S(O)n-(C1-6-alkyl), S(O)n-(C1-6-haloalkyl), C1-6-alkylcarbonylamino, Ph, OCH2Ph, NR6R7; dashed line = single or double bond; R6, R7 = H, C1-6-alkyl, C1-6-hydroxyalkyl, C1-6-haloalkyl, (C1-6-alkoxy)-C1-6-alkyl; n = 0, 1, 2] or their pharmaceutically acceptable salts or solvates; processes for their prepn. comprising reacting piperidine II with sulfonyl deriv. III or reacting sulfonamide IV with KCN and ammonium carbonate; pharmaceutical compns. contg. them; a process for prepg. the pharmaceutical compns.; and their use in therapy. Thus, I [R1 = Me, G1 = 4-cyano-3-methylphenyl, dashed line = double bond] was prepd. from 2-methyl-4-(1,2,3,6-tetrahydropyridin-4-yl)benzonitrile via reaction with [(4S)-4-methyl-2,5-dioxoimidazolodin-4-yl]methnasulfonyl chloride in CH2Cl2/THF contg. EtN(CHMe2)2. The enzyme inhibiting activity of I [R1 = Me, G1 = 4-cyano-3-methylphenyl, dashed line = double bond] was detd. [IC50 = 0.26 nM vs MMP12; IC50 = 15.00 nM vs MMP9].

IT **675107-00-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and deprotection of; prepn. of imidazolidinedione derivs. and their use as metalloproteinase inhibitors in treating obstructive pulmonary disease)

RN 675107-00-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(4-cyano-3-methylphenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

h eb c g cg b cg eb

L9 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | 2 Hits | References

ACCESSION NUMBER: 2004:41442 HCAPLUS
DOCUMENT NUMBER: 140:111281
TITLE: Preparation of substituted piperidines as NK1 receptor ligands
INVENTOR(S): Alvaro, Giuseppe; Cardullo, Francesca; Di, Fabio Romano; Giovannini, Riccardo; Piga, Elisabetta; Tranquillini, Maria Elvira
PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Di Fabio, Romano
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005256	A2	20040115	WO 2003-EP7127	20030702

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-15393 A 20020703
GB 2003-6454 A 20030320

OTHER SOURCE(S): MARPAT 140:111281
GI

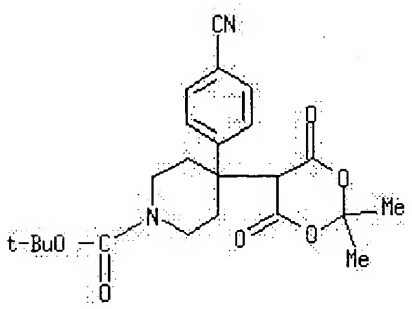
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R = alkyl, cyano, alkoxy, etc.; R1 = H, halo, cycloalkyl, OH, etc.; R2 = H, alkyl; R3-4 = H, CN, alkyl, etc.; R5 = CF3, SO0-2, alkyl, etc.; R6 = H, alkyl; m = 1-4; n = 1-2; p = 0-3; q = 1-3] are prepd. For instance, 4-carboxymethyl-4-(4-fluorophenyl)piperidine-1-carboxylic acid tert-Bu ester (prepn. given) is coupled to 3,5- (DMF, EDCI, HOBt) and deprotected (CH2Cl2, TFA) to give II. Example compds. inhibit (rat) serotonin transporter with pIC50 in the range of 7.50 - 5.30. I are useful in the treatment of conditions mediated by tackykinins and/or by selective inhibition of serotonin reuptake transporter protein.

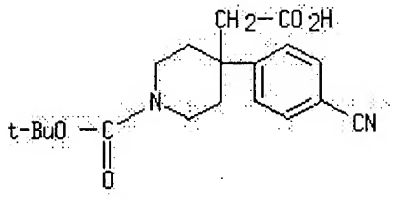
IT **644982-87-6P**, 1,1-Dimethylethyl 4-(4-cyanophenyl)-4-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-1-piperidinecarboxylate **644982-88-7P**, [4-(4-Cyanophenyl)-1-[[(1,1-dimethylethyl)oxy]carbonyl]-4-piperidinyl]acetic acid **644982-89-8P**, 1,1-Dimethylethyl 4-(4-cyanophenyl)-4-[2-[[1-(3,5-dibromophenyl)ethyl](methyl)amino]-2-oxoethyl]-1-piperidinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)

h eb c g cg b cg eb

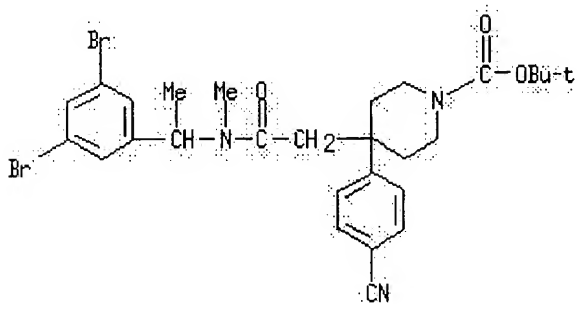
(prepn. of substituted (homo)piperidines as NK1 receptor ligands)
RN 644982-87-6 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-4-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 644982-88-7 HCAPLUS
CN 4-Piperidineacetic acid, 4-(4-cyanophenyl)-1-[(1,1-dimethylethoxy)carbonyl]- (9CI) (CA INDEX NAME)



RN 644982-89-8 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-4-[2-[[1-(3,5-dibromophenyl)ethyl]methylamino]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | More References

ACCESSION NUMBER: 2003:591178 HCAPLUS
DOCUMENT NUMBER: 139:149653
TITLE: Preparation of quinoxaline derivatives as poly(ADP-ribose) polymerase (PARP) inhibitors for treatment of rheumatoid arthritis
INVENTOR(S): Takayama, Kazuhisa; Masuda, Naoyuki; Hondo, Takeshi; Hirabayashi, Ryoji; Seki, Norio; Koga, Yuji; Naito, Ryo; Okamoto, Yoshinori; Kaizawa, Hiroyuki; Okuda, Takao; Okada, Youhei; Takeuchi, Makoto
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2

h eb c g cg b cg eb

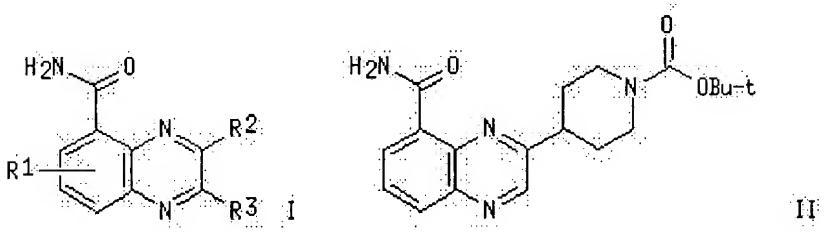
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062234	A1	20030731	WO 2003-JP545	20030122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-14121 A 20020123
OTHER SOURCE(S): MARPAT 139:149653
GI



AB The title quinoxaline derivs. with general formula of I [wherein wherein R1 = H, alkoxy, halo, or (un)substituted alkyl; R2 = halo, (un)substituted OH, SH, or amino, etc.; R3 = H, OH, halo, (un)substituted cycloalkyl, cycloalkenyl, heterocyclyl, or alkyl, etc.; with exclusions] and pharmaceutically acceptable salts thereof are prepd. as poly(ADP-ribose) polymerase (PARP) inhibitors for the treatment of rheumatoid arthritis. For example, the quinoxalinecarboxamide II was prepd. in a four-step synthesis starting from N-(tert-butoxycarbonyl)isonipecotic acid comprising ring formation reaction. Some of compds. I showed IC50 of 3.8-72 nM against human PARP.

IT **569667-98-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of quinoxaline derivs. as PARP inhibitors for treatment of rheumatoid arthritis)

RN 569667-98-7 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[4-(chloroacetyl)phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

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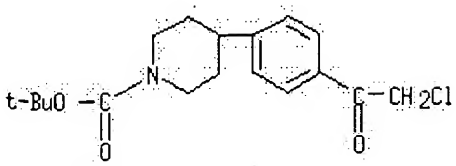


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:754196 HCAPLUS
DOCUMENT NUMBER: 137:257677
TITLE: Methods of treating or preventing Alzheimer's disease using 4-aryl-3-aralkoxypiperidines and -azabicyclooctanes
INVENTOR(S): Nieman, James A.; Fang, Lawrence; Jagodzinska, Barbara
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 449 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

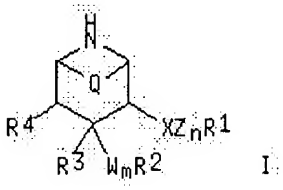
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076440	A2	20021003	WO 2002-US9100	20020321
WO 2002076440	A3	20021128		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-278371P P 20010323
US 2001-308729P P 20010730

OTHER SOURCE(S): MARPAT 137:257677
GI



I

AB Disclosed are methods for treating or preventing Alzheimer's disease, and other diseases, and/or inhibiting β-secretase enzyme, and/or inhibiting deposition of A beta peptide in a mammal, using 3,4-disubstituted piperidinyl compds. (I) wherein the variables R1, R2, R3, R4, Q, W, X, Z, m, and n are defined below. Although neither the compds. nor the methods of prepn. are claimed, ~150 example prepns.,

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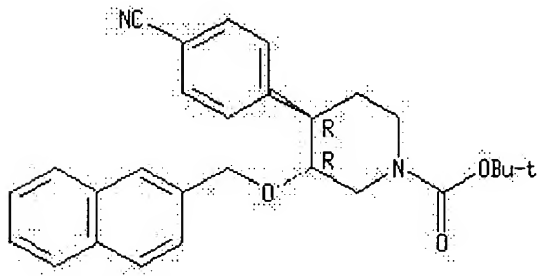
translations from the German examples of patent WO 9709311, are included. I inhibit β-secretase with IC50 < 50 μM; compds. that are effective inhibitors of β-secretase activity demonstrate reduced cleavage of the substrate as compared to a control. In I, R1 is aryl, heterocycle; R2 is Ph, naphthyl, acenaphthyl, cyclohexyl, pyridyl, pyrimidinyl, pyrazinyl, oxopyridinyl, diazinyl, triazolyl, thienyl, oxazolyl, oxadiazolyl, thiazolyl, pyrrolyl, or furyl, optionally substituted. R3 is: H, hydroxy, lower-alkoxy, or lower-alkenyloxy; R4 is: H, lower-alkyl, lower-alkenyl, lower-alkoxy, hydroxy-lower-alkyl, lower-alkoxy-lower-alkyl, benzyl, oxo, or where R3 and R4 together are a bond, or as specified in the claims. Q is: ethylene, or is absent; X is: a bond, -O-, -S-, -CH-R11- (R11 defined in claims), -CHOR9- (R9 defined in claims), -OCO, -CO-, or C:NOR10- (R10 is carboxyalkyl, alkoxycarbonylalkyl, alkyl or H), with the bond emanating from an O or S atom joining to a satd. C atom of group Z or to R1; W is: -O-, or -S-; Z is: lower-alkylene, lower-alkenylene, hydroxy-lower-alkylidene, -O-, -S-, -O-Alk- (Alk is a lower alkylene), -S-Alk-, -Alk-O-, or -Alk-S. N is: 1, or 0 or 1 when X is -O-CO; and where m is 0 or 1; with provisos.

IT **188863-73-2P**, 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-(2-naphthalenylmethoxy)-, 1,1-dimethylethyl ester, trans-
188863-76-5P, 1-Piperidinecarboxylic acid, 3-(2-naphthalenylmethoxy)-4-[4-[[(phenylacetyl)amino]methyl]phenyl]-, 1,1-dimethylethyl ester, trans- **188863-78-7P**, 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-hydroxy-, 1,1-dimethylethyl ester, (3R,4R)-rel- **188863-80-1P**, 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-[[4-[[2-(trimethylsilyl)ethoxy]methoxy]-2-naphthalenyl]methoxy]-, 1,1-dimethylethyl ester, trans-
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(methods of treating or preventing Alzheimer's and other diseases using 4-aryl-3-aralkoxypiperidines and -azabicyclooctanes)

RN 188863-73-2 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-(2-naphthalenylmethoxy)-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

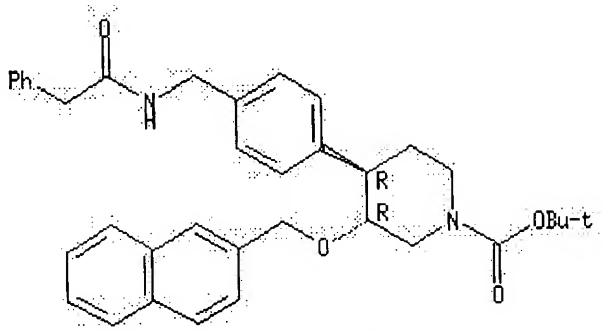
Relative stereochemistry.



RN 188863-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 3-(2-naphthalenylmethoxy)-4-[4-[[(phenylacetyl)amino]methyl]phenyl]-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

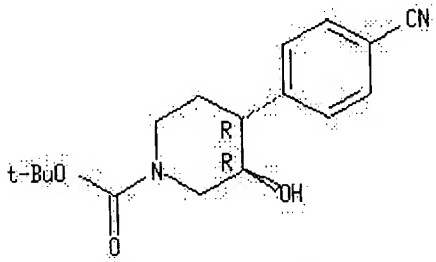
Relative stereochemistry.

h eb c g cg b cg eb



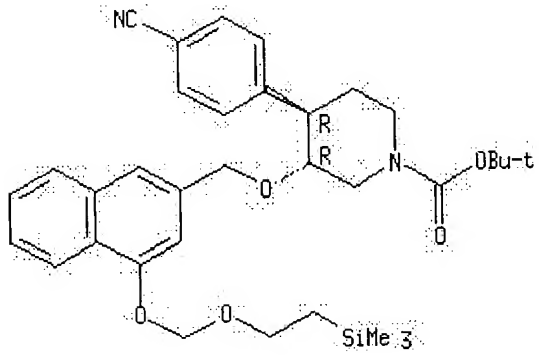
RN 188863-78-7 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-hydroxy-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 188863-80-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-[[4-[[2-(trimethylsilyl)ethoxy]methoxy]-2-naphthalenyl]methoxy]-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L9 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:675993 HCAPLUS
DOCUMENT NUMBER: 137:216874
TITLE: Acylated piperidine derivatives, specifically 1-(pyrrolidinylcarbonyl)piperidines, 1-(piperidinylcarbonyl)piperidines, and analogs, as melanocortin-4 receptor agonists, and their pharmaceutical compositions and therapeutic uses
INVENTOR(S): Ujjainwalla, Feroze; Chu, Lin; Goulet, Mark T.; Lee, Bonnie; Warner, Daniel; Wyvratt, Matthew J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 112 pp.

h eb c g cg b cg eb

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068388	A2	20020906	WO 2002-US5724	20020225
WO 2002068388	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EE 200300415	A	20031215	EE 2003-415	20020225
EP 1383501	A2	20040128	EP 2002-728357	20020225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004529105	T2	20040924	JP 2002-567902	20020225
US 2003225060	A1	20031204	US 2003-356879	20030203
NO 2003003812	A	20031028	NO 2003-3812	20030827
PRIORITY APPLN. INFO.:			US 2001-272258P P	20010228
			US 2001-300118P P	20010622
			WO 2002-US5724 W	20020225

OTHER SOURCE(S): MARPAT 137:216874
GI

10368719 = NO

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Certain novel 4-substituted N-acylated piperidine derivs., specifically I, are agonists of the human melanocortin receptor(s) and, in particular, are selective agonists of the human melanocortin-4 receptor (MC-4R) [wherein: p = 1 or 2; q = 0, 1, or 2; n = 0, 1, or 2; R1 = H, amidino, alkyliminoyl, (un)substituted alkyl, (CH2)n-G1 [G1 = (un)substituted cycloalkyl, Ph, naphthyl, or heteroaryl]; R2 = (un)substituted Ph, naphthyl, or heteroaryl; X = alkyl, (CH2)n-G2 [G2 = (un)substituted cycloalkyl, Ph, naphthyl, heteroaryl, heterocyclyl, cyano, CONH2, CO2H, OH, NH2, and various derivs.] where any of (CH2)n may also be substituted; including pharmaceutically acceptable salts]. They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction. Approx. 180 invention compds. I and approx. 25 intermediates were prepd. For instance, (2-bromo-5-chlorophenyl)acetic acid underwent a sequence of Me esterification, coupling with tert-Bu 4-[[(trifluoromethyl)sulfonyl]oxy]-3,6-dihydropyridine-1(2H)-carboxylate via a boronate ester, removal of the BOC group, and amidation with (3S,4R)-1-(tert-butyl)-4-(2,4-difluorophenyl)pyrrolidine-3-carboxylic acid. The unsatd. amide-ester underwent hydrogenation, sapon. of the ester, and amidation with MeNH2.HCl, to give title compd. II. Representative compds. I bound to cloned human MC-4R in vitro with IC50 values generally below 2 μM, and also acted as agonists toward cloned human MCR in a functional assay with

h eb c g cg b cg eb

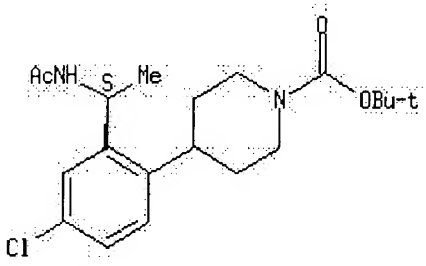
EC50 values less than 1 μM.

IT **455957-92-3P**, tert-Butyl 4-[2-[(1S)-1-(acetylamino)ethyl]-4-chlorophenyl]piperidine-1-carboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of acylated piperidine derivs., particularly (pyrrolidinylcarbonyl)piperidines, (piperidinylcarbonyl)piperidines, and analogs, as melanocortin-4 receptor agonists)

RN 455957-92-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[2-[(1S)-1-(acetylamino)ethyl]-4-chlorophenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:868447 HCAPLUS
DOCUMENT NUMBER: 136:5917
TITLE: Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
INVENTOR(S): Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products Inc., USA
SOURCE: PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

09/843126 =10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090101	A1	20011129	WO 2001-US13811	20010427
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003187020	A1	20031002	US 2001-843126	20010426
EP 1296972	A1	20030402	EP 2001-930925	20010427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011206	A	20030415	BR 2001-11206	20010427

h eb c g cg b cg eb

JP 2004510697	T2	20040408	JP 2001-586288		20010427
NO 2002005601	A	20030106	NO 2002-5601		20021121
ZA 2002009484	A	20040223	ZA 2002-9484		20021121
PRIORITY APPLN. INFO.:			GB 2000-12362	A	20000522
			US 2001-843126	A	20010426
			WO 2001-US13811	W	20010427

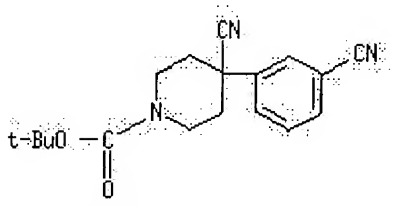
OTHER SOURCE(S): MARPAT 136:5917
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

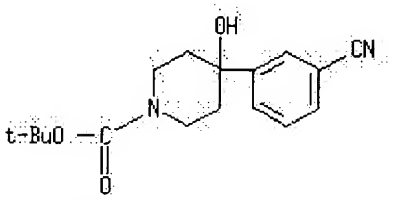
AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are β to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prepd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf)•CH2Cl2, 80°C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

IT **375853-88-6P 375853-96-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors)

RN 375853-88-6 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-(3-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 375853-96-6 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(3-cyanophenyl)-4-hydroxy-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

h eb c g cg b cg eb

L9 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:798195 HCAPLUS
DOCUMENT NUMBER: 135:344381
TITLE: Preparation of 1-aroyl-piperidinyl benzamidines as inhibitors of Factor Xa or tryptase
INVENTOR(S): Pauls, Heinz; Gong, Yong; Levell, Julian; Astles, Peter C.; Eastwood, Paul R.
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081310	A1	20011101	WO 2001-US13810	20010427
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002045613	A1	20020418	US 2001-841417	20010424
EP 1278732	A1	20030129	EP 2001-930924	20010427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531193	T2	20031021	JP 2001-578405	20010427

PRIORITY APPLN. INFO.:

US 2000-200066P	P	20000427
GB 2000-18306	A	20000726
US 2001-841417	A	20010424
WO 2001-US13810	W	20010427

OTHER SOURCE(S): MARPAT 135:344381
GI

09/841,417 11 no

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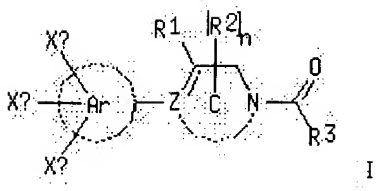

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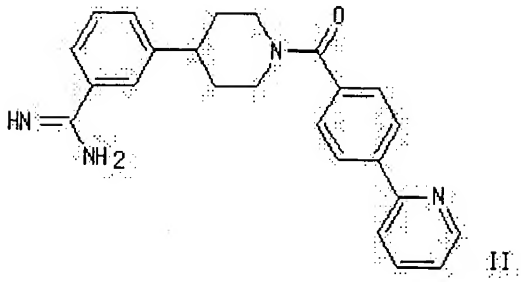


II

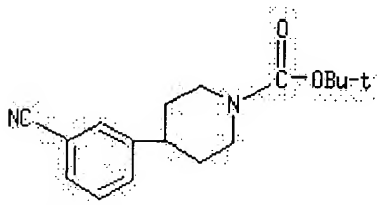
AB The title compds. [I; Z = C, N; ring C = 4-7 membered azaheterocyclyl, 4-7 membered azaheterocyclenyl; Ar = aryl, monocyclic heteroaryl, bicyclic azaheteroaryl; R1 = H, CH2OR12, CH2SR12, etc.; R2 = H, alkyl, aralkyl, etc.; R3 = cycloalkyl, cycloalkenyl, heterocyclyl, etc.; Xa, Xb, Xc = H, (hydroxy)NH, halo, etc.; R12 = H, alkyl, acyl, etc.], useful for the treatment of patients suffering from conditions which can be ameliorated by the administration of an inhibitor of Factor Xa or tryptase, were prepd. E.g., a multi-step synthesis of II.2F3CCO2H which showed Ki of 9.0 nM against Factor Xa, was given.

IT **370864-73-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of 1-aroyl-piperidinyl benzamidines as inhibitors of Factor Xa or tryptase)

RN 370864-73-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(3-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:618024 HCAPLUS
DOCUMENT NUMBER: 135:180954
TITLE: Synthesis of cyclic hexapeptide derivatives for use as antimicrobial or antifungal agents in humans or animals
INVENTOR(S): Toda, Ayako; Matsuya, Takahiro; Mizuno, Hiroaki; Matsuda, Hiroshi; Murano, Kenji; Barrett, David; Ogino, Takashi; Matsuda, Keiji
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan

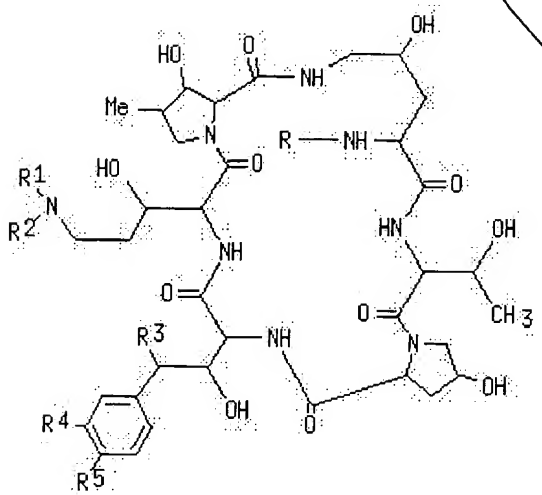
h eb c g cg b cg eb

SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060846	A1	20010823	WO 2001-JP1204	20010220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001034095	A5	20010827	AU 2001-34095	20010220
EP 1259535	A1	20021127	EP 2001-906140	20010220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008792	A	20021203	BR 2001-8792	20010220
JP 2003523349	T2	20030805	JP 2001-560230	20010220
RU 2224765	C1	20040227	RU 2002-125463	20010220
NZ 520808	A	20040326	NZ 2001-520808	20010220
US 2003083238	A1	20030501	US 2002-30161	20020130
NO 2002003697	A	20021014	NO 2002-3697	20020806
ZA 2002006362	A	20031110	ZA 2002-6362	20020808
PRIORITY APPLN. INFO.:			AU 2000-5752 A	20000221
			AU 2000-9552 A	20000821
			AU 2000-2344 A	20001228
			WO 2001-JP1204 W	20010220

OTHER SOURCE(S): MARPAT 135:180954
GI

10030161 = NO



I

AB Cyclic polypeptides [(I); R, R1 (independently) = H, acyl; R2 = hydroxyalkyl; R3 = H, OH; R4 = H, OH, alkoxy, HO3SO-; R5 = OH, acyloxy], useful as antimicrobial or antifungal agents, or as β-1,3-glucan synthase inhibitors (no data), for use in prophylactic and/or therapeutic

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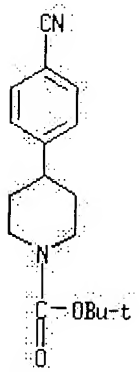
treatment of infectious diseases in humans or animals, were prepd. A variety of substituted acyl R groups were prepd. and coupled with the cyclopeptide. Thus, I [R = 4-[2-[4-[4-[5-methoxypentyloxy]piperidin-1-yl]phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]phenylcarbonyl; R1,R3 = H; R2 = CH(CH2OH)2; R4 = HO3SO; R5 = OH (II)] was prepd. in four steps from the starting protected cyclic peptide sodium salt and activated ester of substituted benzoic acid (prepn. given). In in vitro tests of antimicrobial activity in mouse serum against Candida albicans FP-633, II had MIC <0.3 μg/mL.

IT **162997-33-3P**

RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of cyclic hexapeptide derivs. for use as antimicrobial or antifungal agents in humans or animals)

RN 162997-33-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:513681 HCAPLUS
DOCUMENT NUMBER: 133:120346
TITLE: Preparation of polyazanaphthalenone derivatives useful as alpha 1a adrenoceptor antagonists
INVENTOR(S): Bock, Mark G.; Patane, Michael A.; Steele, Thomas G.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043374	A1	20000727	WO 2000-US1775	20000124

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

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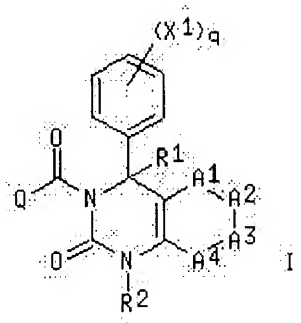
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6358959 B1 20020319 US 2000-481991 20000111

PRIORITY APPLN. INFO.: US 1999-117255P P 19990126

OTHER SOURCE(S): MARPAT 133:120346

GI



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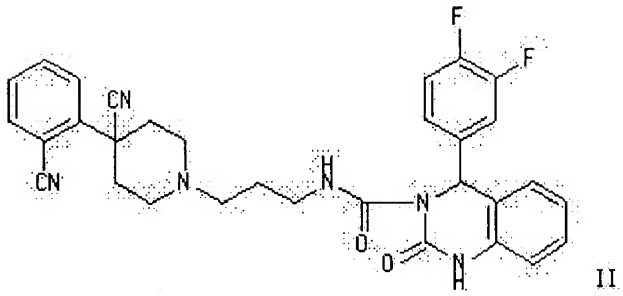


II

AB Dihydroquinazolin-2-one and dihydropteridin-2-one derivs. (I) [wherein Q = (un)substituted piperidinylaminoalkylamino, cycloalkylaminoalkylamino, piperidinylaminoalkypiperidinyl, cycloalkylaminoalkylpiperidinyl, etc.; A1-A4 = independently (un)substituted C or N; X1 = H, halo, CN, NO2, (fluorinated) (cyclo)alkyl, or (un)substituted alkoxy(alkyl); R1 = H, (fluorinated) (cyclo)alkyl, or (un)substituted Ph; R2 = H or (fluorinated) alkyl; q = 0-5] and pharmaceutically acceptable salts were prepd. as alpha 1a adrenergic receptor antagonists for use in the treatment of benign prostatic hyperplasia. For example, II was formed in a multistep sequence. Anthranilonitrile was treated with 3,4-difluorophenyl magnesium bromide, followed by (EtO)2CO, to give the 2(1H)-quinazolinone. The quinazolinone was then N-alkylated with 4-MeOC6H4CH2Cl and hydrogenated with NaBH4. Finally, addn. of 4-NO2C6H4OC(O)Cl, followed by amidation with N-(3-aminopropyl)-4-(2-cyanophenyl)-4-cycanopiperidine•HCl, and deprotection using TFA gave II. I are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype, e.g. the tissue found surrounding the urethral lining, without at the same time inducing hypotension (no data). Therefore, I give acute relief to males suffering from benign prostatic hyperplasia by permitting less hindered urine flow. Combination of I with a human 5-alpha reductase inhibitory compd. provides both acute and chronic relief from the effects of benign prostatic hyperplasia.

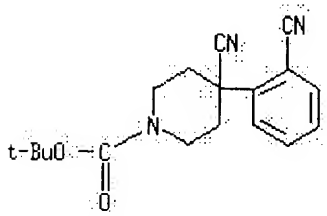
IT 268205-02-3P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)

(prepn of dihydroquinazolin-2-one and dihydropteridin-2-one deriv. 1a adrenoceptor antagonists by treatment of o-amino(hetero)arylnitriles with arylmagnesium bromides, followed by cycloaddn. with (EtO)2CO, and

h eb c g cg b cg eb

further ring substitution)
RN 268205-02-3 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:470758 HCAPLUS
DOCUMENT NUMBER: 133:187580
TITLE: In Vitro and in Vivo Evaluation of Dihydropyrimidinone C-5 Amides as Potent and Selective α1A Receptor Antagonists for the Treatment of Benign Prostatic Hyperplasia
AUTHOR(S): Barrow, James C.; Nantermet, Philippe G.; Selnick, Harold G.; Glass, Kristen L.; Rittle, Kenneth E.; Gilbert, Kevin F.; Steele, Thomas G.; Homnick, Carl F.; Freidinger, Roger M.; Ransom, Rick W.; Kling, Paul; Reiss, Duane; Broten, Theodore P.; Schorn, Terry W.; Chang, Raymond S. L.; O'Malley, Stacey S.; Olah, Timothy V.; Ellis, Joan D.; Barrish, Andrea; Kassahun, Kelem; Leppert, Paula; Nagarathnam, Dhanapalan; Forray, Carlos
CORPORATE SOURCE: Departments of Medicinal Chemistry Pharmacology and Drug Metabolism, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(14), 2703-2718
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB α1 Adrenergic receptors mediate both vascular and lower urinary tract tone, and α1 receptor antagonists such as terazosin are used to treat both hypertension and benign prostatic hyperplasia (BPH). Recently, three different subtypes of this receptor have been identified, with the α1A receptor being most prevalent in lower urinary tract tissue. This paper explores 4-aryldihydropyrimidinones attached to an aminopropyl-4-arylpiperidine via a C-5 amide as selective α1A receptor subtype antagonists. In receptor binding assays, these types of compds. generally display Ki values for the α1a receptor subtype of <1nM, while being greater than 100-fold selective vs. the α1b and α1d receptor subtypes. Many of these compds. were also evaluated in vivo and found to be more potent than terazosin in both a rat model of prostate tone and a dog model of intra-urethral pressure without significantly affecting blood pressure. While many of the compds. tested displayed poor pharmacokinetics, (4R)-4-(3,4-difluorophenyl)-6-methoxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid

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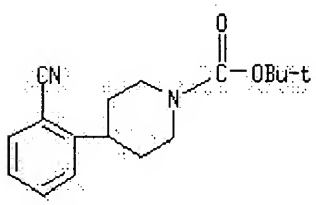
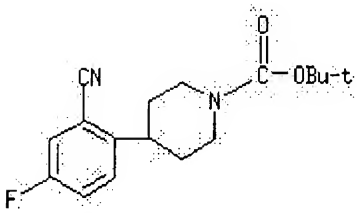
[3-[4-(4-fluorophenyl)piperidin-1-yl]propyl]amide (I) was found to have adequate bioavailability (>20%) and half-life (>6 h) in both rats and dogs. Due to its selectivity for the α1a over the α1b and α1d receptors, as well as its favorable pharmacokinetic profile, I has the potential to relieve the symptoms of BPH without eliciting effects on the cardiovascular system.

IT **256951-72-1P 256951-76-5P 256951-83-4P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and properties and reactions of; prepn. of dihydropyrimidinone C-5 amides as potent and selective α1A receptor antagonists for the treatment of benign prostatic hyperplasia in relation to)

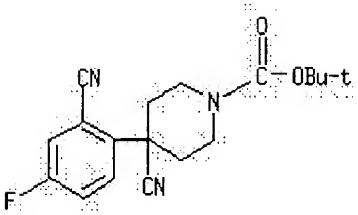
RN 256951-72-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 256951-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 256951-83-4 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

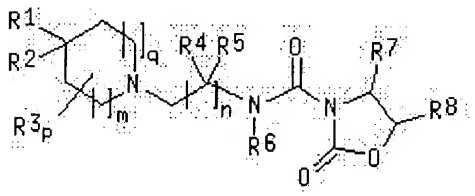
ACCESSION NUMBER: 2000:335394 HCAPLUS
DOCUMENT NUMBER: 132:334452
TITLE: Preparation of oxazolidinones useful as α1-adrenoceptor antagonists
INVENTOR(S): Nerenberg, Jennie B.; Bock, Mark G.; Selnick, Harold

h eb c g cg b cg eb

G.; Payne, Linda
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027827	A1	20000518	WO 1999-US26437	19991109
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6319932	B1	20011120	US 1999-438006	19991110
PRIORITY APPLN. INFO.:			US 1998-107839P P	19981110
			US 1998-190506 A	19981112

OTHER SOURCE(S): MARPAT 132:334452
GI



I

AB Prepn. of oxazolidinones I [R1 = = (un)substituted Ph, naphthyl, heterocyclyl, etc.; R2 = H, CN, OH, etc.; R3 = alkyl; R4, R5 = H, alkyl, cycloalkyl; R6 = H, alkyl; R7 = (un)substituted Ph, pyridyl, thienyl, etc.; R8 = CONH2, CORc, etc.; m, q = 0-2; n = 1-3; p = 0-2], and their use as α1-adrenergic receptor antagonists, are described. One application of these compds. is in the treatment of benign prostatic hyperplasia. Another utility of I is provided by combination with a human 5-alpha reductase inhibitory compd., such that both acute and chronic relief from the effects of benign prostatic hyperplasia can be achieved. E.g., (4S,5R)-4-(3,4-difluorophenyl)-2-oxooxazolidine-3,5-dicarboxylic acid 5-amide 3-({3-[4-(4-fluorophenyl)piperidin-1-yl]propyl}amide) was prepd.

IT **256951-72-1P 256951-76-5P 268205-02-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of oxazolidinones useful as α1-adrenoceptor antagonists)

RN 256951-72-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

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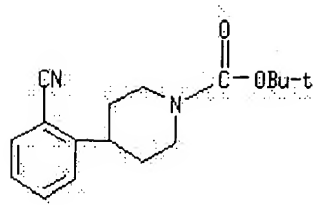
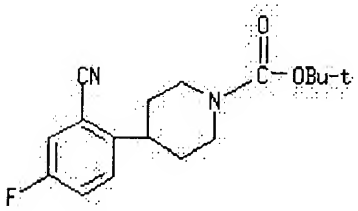
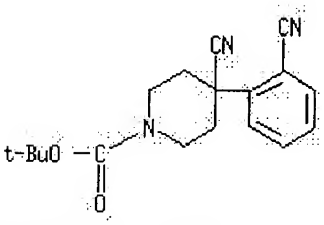


RN 256951-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 268205-02-3 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | More References

ACCESSION NUMBER: 2000:335386 HCAPLUS
DOCUMENT NUMBER: 132:334451
TITLE: Preparation of oxazolidin-2-one-3-carboxamides as α1A adrenoceptor antagonists
INVENTOR(S): Nerenberg, Jennie B.; Bock, Mark G.; Patane, Michael A.; Selnick, Harold G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027817	A1	20000518	WO 1999-US26438	19991109

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

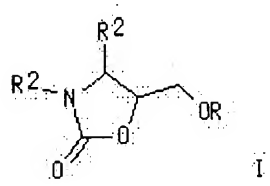
h eb c g cg b cg eb

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6228870	B1	20010508	US 1999-437841		19991110
PRIORITY APPLN. INFO.:			US 1998-107838P	P	19981110
			US 1998-190505	A	19981112

OTHER SOURCE(S): MARPAT 132:334451

GI



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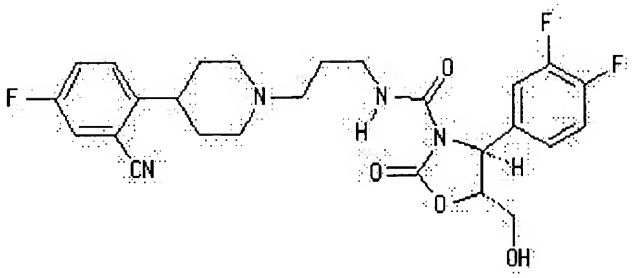


II

AB Title compds. [I; R = H, alkyl, Z1CF3; R1 = (un)substituted Ph; R2 = R3Z(CH2)nNHCO; R3 = (un)substituted Ph or -2-pyridyl; Z = 4-(un)substituted piperidine-4,1-diyl; Z1 = (CH2)1-4; n = 2-4] were prepd. Thus, (4S,5R)-I [R = THP, R1 = C6H3F2-3,4, R2 = CO2C6H4(NO2)-4] was amidated by 4,3-F(NC)C6H3Z(CH2)3NH2 (Z = piperidine-4,1-diyl)(prepn. each given) and the product deprotected to give title compd. II. Data for biol. activity of I were given.

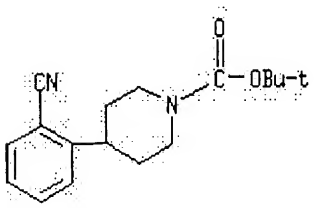
IT **256951-72-1P 256951-76-5P 268205-02-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)

(prepn. of oxazolidin-2-one-3-carboxamides as α1A adrenoceptor antagonists)

RN 256951-72-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 256951-76-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

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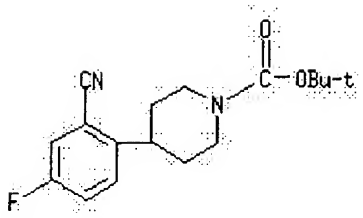
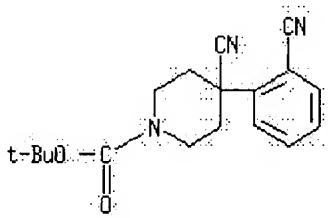


RN 268205-02-3 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:314542 HCAPLUS
DOCUMENT NUMBER: 132:308252
TITLE: Preparation of dihydropyridinones and pyrrolinones useful as alpha 1a adrenoceptor antagonists
INVENTOR(S): Barrow, James; Selnick, Harold G.; Nanterment, Philippe G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000025782	A1	20000511	WO 1999-US24990		19991025
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6235759	B1	20010522	US 1999-428973		19991028
PRIORITY APPLN. INFO.:			US 1998-106095P	P	19981029
			US 1999-141463P	P	19990629

OTHER SOURCE(S): MARPAT 132:308252
GI

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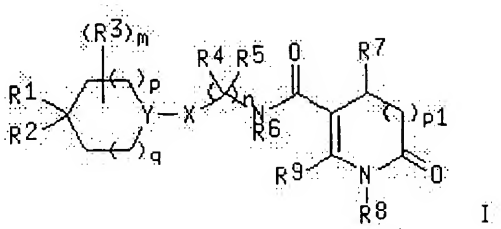

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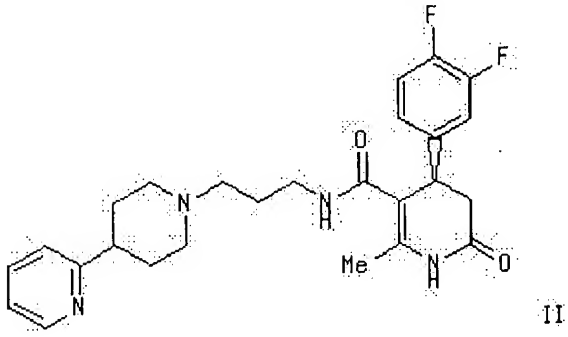


II

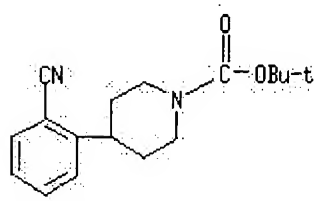
AB Novel dihydropyridinone and pyrrolinone compds. [I; Y = CH or N; X = CR4R5, when Y = N; X = NR6, when Y = CH; R1 = Ph, mono- or poly-substituted Ph, naphthyl, mono- or poly-substituted naphthyl, heterocyclic, or mono- or poly-substituted heterocyclic; wherein the heterocyclic is selected from the group consisting of pyridyl, pyrazinyl, thienyl, thiazolyl, furanyl and quinazolinyl; R2 = H, cyano, hydroxy, C1-6 alkoxy, CO2Rc, C(O)N(Rc)2, tetrazole, isooxadiazole, Ph, mono- or poly-substituted Ph, naphthyl, mono- or poly-substituted naphthyl, heterocyclic, or mono- or poly-substituted heterocyclic; wherein the heterocyclic is selected from the group consisting of pyridyl, thienyl and furanyl; R3 = a substituent connected to a ring atom other than CR1R2 or Y which is independently C1-4 alkyl; R4, R5 = H, C1-6 alkyl, C3-8 cycloalkyl; R6 = H, C1-4 alkyl; R7 = Ph, or mono- or poly-substituted phenyl; R8 = H, C1-6 alkyl, (CH2)0-4CO2Rc, (CH2)0-4C(O)Rc; R9 = H, halo, cyano, C1-6 alkyl, C3-8 cycloalkyl, C1-6 alkoxy, halogenated C1-6 alkyl, halogenated C3-8 cycloalkyl, halogenated C1-6 alkoxy, (CH2)1-4ORb, CO2Rc, C(O)Rc, or C(O)N(Rc)2; Rb, Rc = H, C1-6 alkyl, halogenated C1-6 alkyl; m = 0-2; n = 2-4, when X = NR6; n = 1-3, when X = CR4R5; p1 = 0 or 1, provided that when Y = N, p1 = 0; p, q = 0-2, p+q≤3] or pharmaceutically acceptable salts thereof are prepd. Their use as alpha 1a adrenergic receptor antagonists is also described (no data). One application of these compds. is in the treatment of benign prostatic hyperplasia. These compds. are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compds. is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compds. is provided by combination with a human 5-alpha reductase inhibitory compd., such that both acute and chronic relief from the effects of benign prostatic hyperplasia can be achieved. Thus, 3-[4-(2-pyridyl)piperidin-1-yl]propylamine was condensed with (R)-(-)-4-(3,4-difluorophenyl)-6-methyl-3,4-dihydro-2-pyridinone-5-carboxylic using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 1-hydroxy-7-azabenenetriazole, and Et3N in DMF to give title compd. (II).

IT **256951-72-1P**, 2-(1-(tert-Butoxycarbonyl)piperidin-4-yl)benzonitrile **256951-76-5P**, 4-(2-Cyano-4-fluorophenyl)piperidine-1-carboxylic acid tert-butyl ester **256951-83-4P**, 4-Cyano-4-(2-cyano-4-fluorophenyl)piperidine-1-carboxylic acid tert-butyl ester

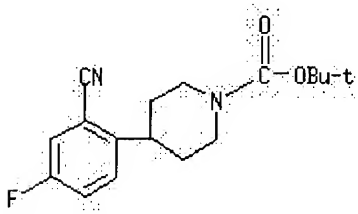
h eb c g cg b cg eb

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of dihydropyridinones and pyrrolinones useful as alpha 1a adrenoceptor antagonists for treatment of benign prostatic hyperplasia)

RN 256951-72-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 256951-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 256951-83-4 HCAPLUS
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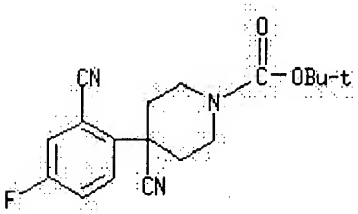

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:98550 HCAPLUS
DOCUMENT NUMBER: 132:137405
TITLE: 2-Oxo-N-(3-piperidinylpropyl)tetrahydropyrimidine-5-carboxamide derivatives as α1a adrenergic receptor antagonists
INVENTOR(S): Barrow, James C.; Nantermet, Philippe G.; Selnick, Harold G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

h eb c g cg b cg eb

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000006565	A1	20000210	WO 1999-US16998		19990727
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9952348	A1	20000221	AU 1999-52348		19990727
US 6339090	B1	20020115	US 1999-363631		19990729
PRIORITY APPLN. INFO.:			US 1998-94600P	P	19980730
			GB 1998-22364	A	19981013
			WO 1999-US16998	W	19990727

OTHER SOURCE(S): MARPAT 132:137405

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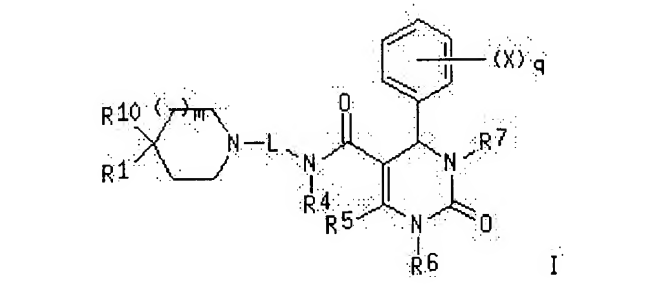

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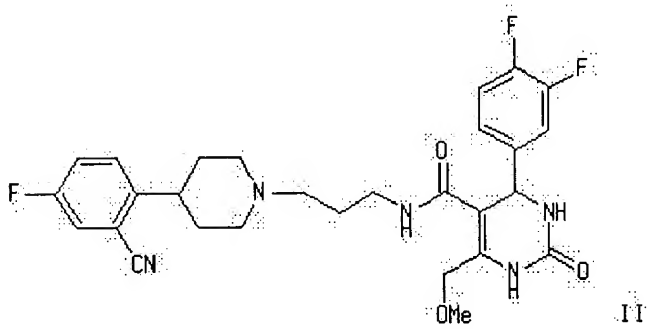

II

AB Title compds. (I) [wherein R1 = (un)substituted Ph or pyridyl; R2 = (cyclo)alkyl or trifluoromethyl(alkyl); R4 = H, alkyl, or trifluoromethyl(alkyl); R5 = H, (alkoxy)alkyl, or trifluoromethyl(alkyl); R6 = H or alkyl; R7 = H, (alkoxy)alkyl, alkoxycarbonyl, acyl, or trifluoromethyl(alkyl); R8 and R9 = independently (cyclo)alkyl or trifluoromethyl(alkyl); R10 = H, OH, CN, alkyl, alkoxy(alkyl), or trifluoromethyl(alkyl); L = (CH2)n, (CHR2)n, CR8R9(CH2)n-1, (CH2)n-1R8R9, CH2CR8R9CH2, CH2CH2CR8R9CH2, or CH2CR8R9CH2CH2; X = independently halo, CN, or alkyl; m = 0-2; n = 2-4; q = 0-4] were prepd. for use in the treatment of benign prostatic hyperplasia. Over fifty target compds. were synthesized and tested for α1a adrenergic receptor binding and selectivity. For example, 4-(R)-(3,4-difluorophenyl)-6-methoxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid was amidated with 2-[1-(3-aminopropyl)piperidin-4-yl]-5-fluorobenzonitrile.2HCl (prepn. given) in the presence of TEA, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimi

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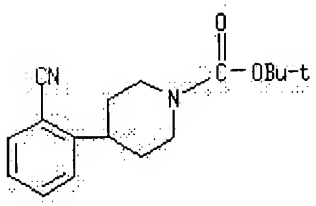
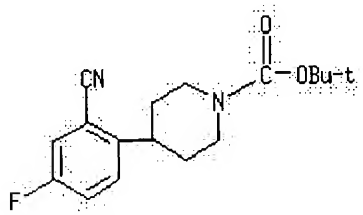
de.HCl, and 1-hydroxybenzotriazole.H2O in DMF to yield (4R)-II. All tested compds. bound to transfected human α1a cell line (ATCC CRL 11140) with Ki ≤ 30 nM and were at least 10 fold more selective in binding to α1a receptors vs. binding to α1b or α1d receptors. Thus, these compds. are selective in their ability to relax smooth muscle tissue enriched in the α1a receptor subtype without at the same time inducing hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the invention compds. is to provide acute relief to males suffering from benign prostatic hyperplasia by permitting less hindered urine flow. These compds. may also be used in combination with a human 5α reductase inhibitory compd., such as finasteride, to provide both acute and chronic relief from the effects of benign prostatic hyperplasia.

IT **256951-72-1P** **256951-76-5P**, 4-(2-Cyano-4-fluorophenyl)piperidine-1-carboxylic acid tert-butyl ester
256951-83-4P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; prepn. of 2-oxo-N-(3-piperidinylpropyl)tetrahydropyrimidine-5-carboxamide derivs. as α1a adrenergic receptor antagonists for the treatment of benign prostatic hyperplasia)

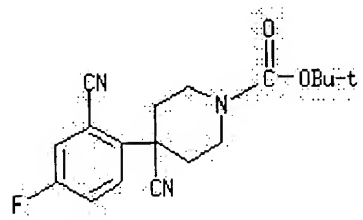
RN 256951-72-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 256951-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 256951-83-4 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-(2-cyano-4-fluorophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

h eb c g cg b cg eb

L9 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Other References

ACCESSION NUMBER: 2000:84383 HCAPLUS
DOCUMENT NUMBER: 132:122515
TITLE: Preparation of thienylphenylpropylamides, -carbamates, -ureas, and related compounds as glutamate receptor potentiators.
INVENTOR(S): Arnold, Macklin Brian; Bleisch, Thomas John; Ornstein, Paul Leslie; Zarrinmayeh, Hamideh; Zimmerman, Dennis Michael; Bender, David Michael; Jones, Winton Dennis
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: Eur. Pat. Appl., 82 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 976744	A1	20000202	EP 1999-305981	19990728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2338916	AA	20000210	CA 1999-2338916	19990728
WO 2000006156	A1	20000210	WO 1999-US17126	19990728
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9951344	A1	20000221	AU 1999-51344	19990728
JP 2002521442	T2	20020716	JP 2000-562011	19990728
US 6617351	B1	20030909	US 2001-744412	20010123
US 2004097499	A1	20040520	US 2003-613684	20030703
PRIORITY APPLN. INFO.:			US 1998-94997P	P 19980731
			WO 1999-US17126	W 19990728
			US 2001-744412	A3 20010123

OTHER SOURCE(S): MARPAT 132:122515

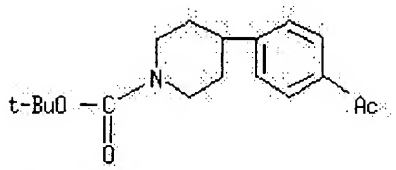
AB R1CR5R8(CR6R7)qBR2 [B = CONRa, NRaCONRa; Ra = H, alkyl; q = 0, 1; R1 = (substituted) naphthyl, Ph, furyl, thienyl, pyridyl; R2 = H, alkyl, cycloalkyl, fluoroalkyl, alkenyl, alkoxyalkyl, phenylalkyl, heteroaryl, (substituted) Ph, etc.; R5-R8 = H, alkyl, aralkyl, alkenyl, aralkenyl, aryl], were prepd. as nervous system agents (no data). Thus, (R)-2-(4-bromophenyl)-N-(tert-butoxycarbonyl)propylamine (prepn. given) was stirred with K2CO3, Pd(Ph3P)4, and thiophene-3-boronic acid in dioxane/H2O at 100° for 4 h to give 66% 2-[4-(3-thienyl)phenyl]propylamine trifluoroacetate. The latter in CH2Cl2 was treated with Et3N and MeO2CCl to give 2-[4-(3-thienyl)phenyl]-N-(methoxycarbonyl)propylamine.

IT **256381-04-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of thienylphenylpropylamides, -carbamates, -ureas, and related compds. as glutamate receptor potentiators)

RN 256381-04-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-acetylphenyl)-, 1,1-dimethylethyl ester

h eb c g cg b cg eb

(9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

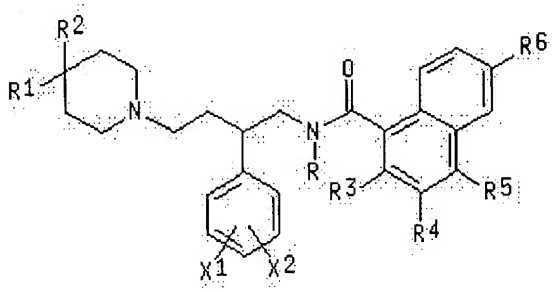
ACCESSION NUMBER: 2000:53591 HCAPLUS
DOCUMENT NUMBER: 132:93213
TITLE: Preparation of N-substituted naphthalenecarboxamides as neurokinin-receptor antagonists
INVENTOR(S): Bernstein, Peter Robert; Dedinas, Robert Frank; Russell, Keith; Shenvi, Ashokkumar Bhikkappa
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002859	A1	20000120	WO 1999-GB2178	19990707
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2336806	AA	20000120	CA 1999-2336806	19990707
AU 9946378	A1	20000201	AU 1999-46378	19990707
BR 9912013	A	20010410	BR 1999-12013	19990707
EP 1097137	A1	20010509	EP 1999-929597	19990707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002520316	T2	20020709	JP 2000-559090	19990707
EP 1433783	A2	20040630	EP 2004-6920	19991004
EP 1433783	A3	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, MK, CY				
US 6365602	B1	20020402	US 2001-743335	20010105
NO 2001000151	A	20010305	NO 2001-151	20010109
ZA 2001002651	A	20020701	ZA 2001-2651	20010330
ZA 2001002658	A	20020701	ZA 2001-2658	20010330
PRIORITY APPLN. INFO.:			GB 1998-14886 A	19980710
			GB 1998-21699 A	19981007
			GB 1998-21703 A	19981007
			GB 1999-9840 A	19990430

h eb c g cg b cg eb

GB 1999-6278	A	19990317
GB 1999-9839	A	19990430
WO 1999-GB2178	W	19990707
EP 1999-947738	A3	19991004

OTHER SOURCE(S): MARPAT 132:93213
GI

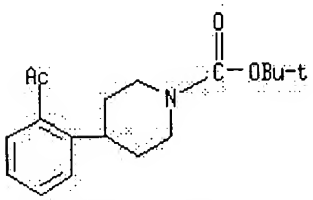


I

AB The title compds. [I; R = alkyl; R1 = (un)substituted Ph, 2-oxo-tetrahydro-1(2H)-pyrimidinyl, 2-oxo-1-piperidinyl; R2 = H, alkoxy, alkanoyloxy, etc.; X1, X2 = H, halo, provided that at least one of X1 or X2 = halo; R3-R6 = H, CN, NO2, etc.] which are antagonists of at least one tachykinin receptor and are useful in the treatment of depression, anxiety, asthma, pain, inflammation, urinary incontinence and other disease conditions, were prepd. and formulated. E.g., a multi-step synthesis of N-[(S)-2-(3,4-dichlorophenyl)-4-{4-[(S)-2-methylsulfonylphenyl]-1-piperidinyl}butyl]-N-methyl-3-cyano-1-naphthamide [(S,S)-I; R = Me; R1 = 2-(MeSO)C6H4; R2 = H; R3 = R5 = R6 = H; R4 = CN; X1 = 3-Cl; X2 = 4-Cl] which showed a dose ratio (P/A) of 32.5 (2 h) and 21.4 (2 h) in NK1 and NK2 in vivo functional assay, resp., was given.

IT **255050-91-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of N-substituted naphthalenecarboxamides as neurokinin-receptor antagonists)

RN 255050-91-0 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(2-acetylphenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

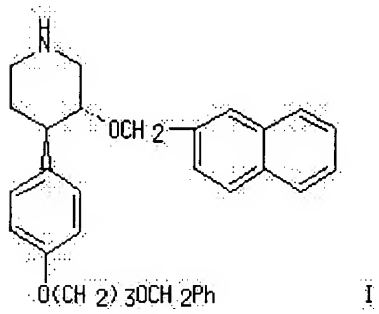
ACCESSION NUMBER: 1999:348249 HCAPLUS
DOCUMENT NUMBER: 131:102177
TITLE: Substituted piperidines - highly potent renin inhibitors due to induced fit adaptation of the active site
AUTHOR(S): Vieira, Eric; Binggeli, Alfred; Breu, Volker; Bur, Daniel; Fischli, Walter; Guller, Rolf; Hirth, Georges;

h eb c g cg b cg eb

Marki, Hans Peter; Muller, Marcel; Oefner, Christian; Scalone, Michelangelo; Stadler, Heinz; Wilhelm, Maurice; Wostl, Wolfgang

CORPORATE SOURCE: Pharma Research Departments, F. Hoffmann-La Roche Ltd, Basel, CH-4070, Switz.

SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(10), 1397-1402
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



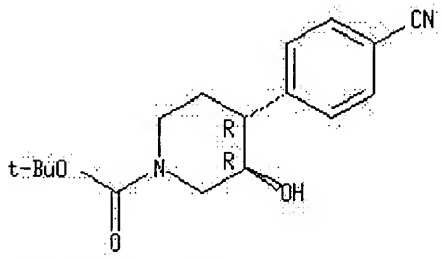
I

AB The identification, synthesis and activity of a novel class of piperidine renin inhibitors, e.g., I, is presented. The most active compds. show activities in the picomolar range and are among the most potent renin inhibitors ever identified.

IT **188863-78-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(piperidine renin inhibitors)

RN 188863-78-7 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-hydroxy-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:102848 HCAPLUS
DOCUMENT NUMBER: 128:167360
TITLE: Preparation of quinoline sulfide derivatives as selective antibacterial agents for Helicobacter pylori
INVENTOR(S): Kawashima, Seiichiro; Terada, Sumio; Saito, Ken-ichi; Suzuki, Toshiaki; Sasahara, Hiroya; Kanda, Toshihisa;

h eb c g cg b cg eb

Inoue, Tsuneo
PATENT ASSIGNEE(S): Zenyaku Kogyo Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804529	A1	19980205	WO 1997-JP2641	19970730
W: AU, CA, CN, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2261903	AA	19980205	CA 1997-2261903	19970730
AU 9737069	A1	19980220	AU 1997-37069	19970730
AU 711654	B2	19991021		
EP 926139	A1	19990630	EP 1997-933841	19970730
R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
US 6057447	A	20000502	US 1999-147605	19990201
PRIORITY APPLN. INFO.:			JP 1996-200466 A	19960730
			WO 1997-JP2641 W	19970730

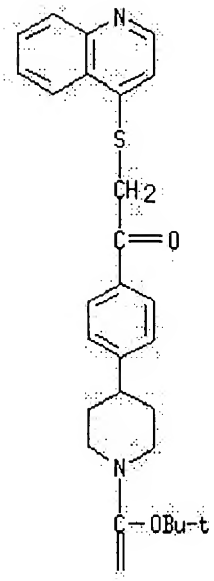
OTHER SOURCE(S): MARPAT 128:167360
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Quinoline sulfide derivs. represented by formula [I; R1 = H, halo, C1-6 alkoxy, C1-6 alkylthio, or di(C1-6 alkyl)amino; R2, R3 = H or C1-6 alkyl; any one of R4 and R5 represents a hydroxyl group with the other representing a hydrogen atom, or alternatively CR4R5 may represent a carbonyl group; m = an integer of 1 or 2; n = an integer of 0 or 1], which are useful for treating or preventing recurrence of stomach or duodenum ulcer and chronic inflammation of stomach related to infection with H. pylori, are prepd. by reacting a quinoline-4(1H)-thione deriv. with a halogen compd. Thus, quinoline-4(1H)-thione and K2CO3 were suspended in acetone, followed by adding 1-benzyloxy-4-bromoacetylbenzene and the resulting mixt. was stirred at room temp. overnight to give 4-[2-(4-benzyloxyphenyl)-2-oxoethylthio]quinoline (II). II and the compd. (III) showed min. inhibitory concn. of 0.05 and 0.004 μg/mL, resp., against H. pylori.

IT **202814-29-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. of quinoline sulfide derivs. as selective antibacterial agents for Helicobacter pylori)
RN 202814-29-7 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[4-[(4-quinolinylthio)acetyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:307688 HCAPLUS
DOCUMENT NUMBER: 126:277402
TITLE: New 4-aryl-3-aralkoxypiperidines and -azabicylooctanes for treating heart and kidney insufficiency
INVENTOR(S): Binggeli, Alfred; Breu, Volker; Bur, Daniel; Fischli, Walter; Gueller, Rolf; Hirth, Georges; Maerki, Hans-Peter; Mueller, Marcel; Oefner, Christian; Stadler, Heinz; Vieira, Eric; Wilhelm, Maurice; Wostl, Wolfgang
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 492 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

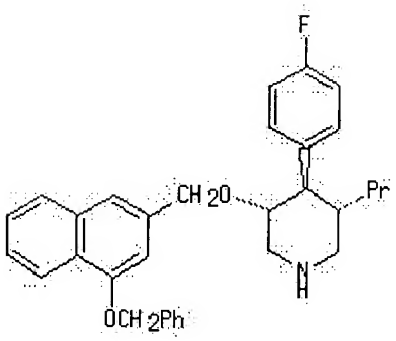
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709311	A1	19970313	WO 1996-EP3803	19960829
W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, TR				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2230931	AA	19970313	CA 1996-2230931	19960829
AU 9667432	A1	19970327	AU 1996-67432	19960829
AU 708616	B2	19990805		
EP 863875	A1	19980916	EP 1996-927715	19960829
EP 863875	B1	20030604		

h eb c g cg b cg eb

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

CN 1202152	A	19981216	CN 1996-197674		19960829
JP 11500447	T2	19990112	JP 1996-510837		19960829
BR 9610385	A	19990706	BR 1996-10385		19960829
NZ 315677	A	20000228	NZ 1996-315677		19960829
RU 2167865	C2	20010527	RU 1998-106388		19960829
AT 242213	E	20030615	AT 1996-927715		19960829
IL 123293	A1	20030624	IL 1996-123293		19960829
CZ 292327	B6	20030917	CZ 1998-684		19960829
PT 863875	T	20031031	PT 1996-927715		19960829
ES 2201192	T3	20040316	ES 1996-927715		19960829
ZA 9607424	A	19970307	ZA 1996-7424		19960902
TW 474932	B	20020201	TW 1996-85110684		19960902
NO 9800954	A	19980428	NO 1998-954		19980305
US 6051712	A	20000418	US 1999-255185		19990222
US 6150526	A	20001121	US 1999-456283		19991207
PRIORITY APPLN. INFO.:			CH 1995-2548	A	19950907
			CH 1996-1876	A	19960726
			WO 1996-EP3803	W	19960829
			US 1996-711339	A3	19960906
			US 1999-255185	A1	19990222

OTHER SOURCE(S): MARPAT 126:277402
GI



I

AB New piperidine and azabicyclooctane derivs. (> 1000 compds.) are renin inhibitors for treatment of high blood pressure, heart and kidney insufficiency. Thus, the piperidine deriv. I was prepd. from 1-benzyl-3-propyl-4-piperidinone by reaction with 4-FC6H4Br, followed by 1-benzyloxy-3-chloromethylnaphthalene and deblocking. I had a renin-inhibiting IC50 of 0.317 μM.

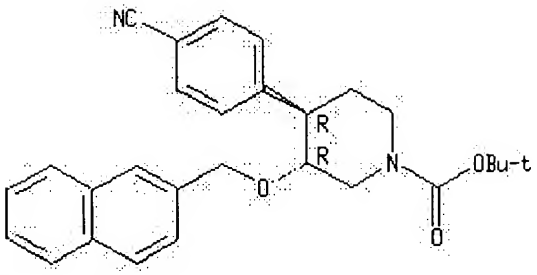
IT **188863-73-2P 188863-76-5P 188863-78-7P 188863-80-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of piperidine and azabicyclooctane derivs. as renin inhibitors)

RN 188863-73-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-(2-naphthalenylmethoxy)-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

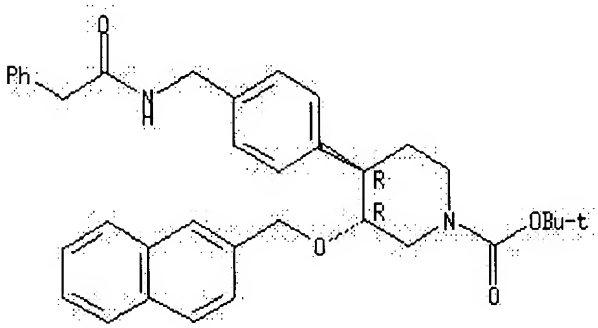
Relative stereochemistry.

h eb c g cg b cg eb



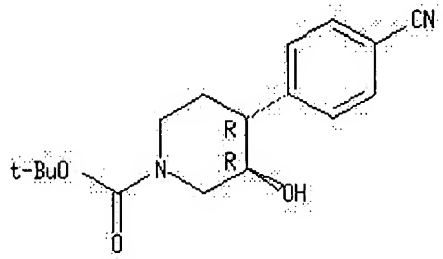
RN 188863-76-5 HCAPLUS
CN 1-Piperidinecarboxylic acid, 3-(2-naphthalenylmethoxy)-4-[4-[[(phenylacetyl)amino]methyl]phenyl]-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 188863-78-7 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-hydroxy-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

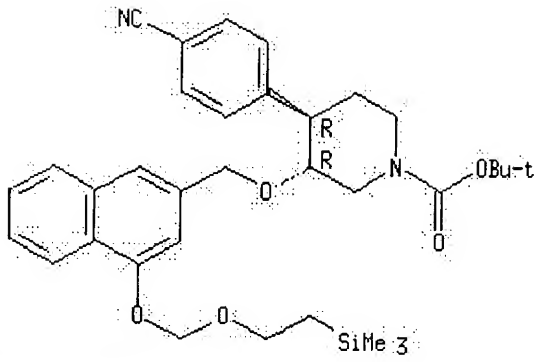
Relative stereochemistry.



RN 188863-80-1 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-3-[[4-[[2-(trimethylsilyl)ethoxy]methoxy]-2-naphthalenyl]methoxy]-, 1,1-dimethylethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

h eb c g cg b cg eb



L9 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:546553 HCAPLUS
DOCUMENT NUMBER: 122:290875
TITLE: Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
INVENTOR(S): Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4234295	A1	19940414	DE 1992-4234295	19921012
EP 592949	A2	19940420	EP 1993-116244	19931007
EP 592949	A3	19940810		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2108093	AA	19940413	CA 1993-2108093	19931008
JP 06199788	A2	19940719	JP 1993-252019	19931008
FI 9304460	A	19940413	FI 1993-4460	19931011
NO 9303647	A	19940413	NO 1993-3647	19931011
NO 180232	B	19961202		
NO 180232	C	19970312		
AU 9348939	A1	19940428	AU 1993-48939	19931011
AU 668765	B2	19960516		
ZA 9307502	A	19950411	ZA 1993-7502	19931011
CN 1087904	A	19940615	CN 1993-118925	19931012
US 5442064	A	19950815	US 1993-135041	19931012
PRIORITY APPLN. INFO.:			DE 1992-4234295 A	19921012

OTHER SOURCE(S): MARPAT 122:290875

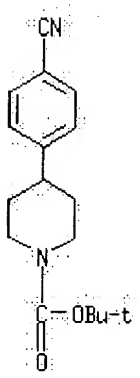
AB ABCDEFG [A = amino(alkyl), C(:NH)NH2, NHC(:NH)NH2, etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene, etc.; D = CH2, CH2CH2, CO, CH2CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E ≠ piperazinylene); G = CO2R5; R5 = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O2N)C6H4O2CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-

h eb c g cg b cg eb

(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC50 of 4.300nM against platelet aggregation in vitro.

IT **162997-33-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. of (di)azine-contg. cyclohexanecarboxylates and analogs as platelet aggregation inhibitors)

RN 162997-33-3 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-(4-cyanophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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FILE 'REGISTRY' ENTERED AT 15:21:10 ON 29 SEP 2004

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L2            1 S L1
L3           24 S L1 FULL

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L4            1 S L3/THU

     FILE 'REGISTRY' ENTERED AT 15:29:06 ON 29 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 15:29:32 ON 29 SEP 2004
L5           22 S L3/PREP

     FILE 'REGISTRY' ENTERED AT 15:31:56 ON 29 SEP 2004
L6              STRUCTURE UPLOADED
L7         8381 S L6 FULL

     FILE 'HCAPLUS' ENTERED AT 15:45:57 ON 29 SEP 2004
L8            1 S L5 AND BOICE, G?/AU
L9           21 S L5 NOT L8
L10           0 S L9 AND CONRAD, K?/AU
L11           0 S L9 AND CORLEY, E?/AU
L12           0 S L9 AND MATTY, L?/AU
L13           0 S L9 AND MURRY, J?/AU
L14           0 S L9 AND SAVARIN, C?/AU

     FILE 'CAOLD' ENTERED AT 15:49:50 ON 29 SEP 2004

=> s l3
L15           0 L3

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h eb c g cg b cg eb